KEY FINDINGS

The key findings of this research are summarized in the table below

Product	Manufacturing Sites and Capacity	Date of Full Production	Launch Dates
Kogenate FS®	Berkeley, CA <500 MAU Expanded capacity <500 MAU Wuppertal, Germany 750 MAU	In production 2002 2005	EU 1Q0[illegible] NA 4Q0[illegible] Japan 200[illegible] Australia 4Q0[illegible] NZ [illegible]
Refacto®	Stockholm,Sweden <250MAU St Louis, MO Unknown Dublin, Ireland Unknown	In production 2002 2004	EU [illegible] NA [illegible] [illegible]effective 4Q0[illegible] Japan [illegible] filing Australia No schedule NZ No schedule
Recombinate®	Thousand Oaks, CA 750-825MAU Neuchatel,Swit 750-1000MAU On contract from GI 2000 380MAU 2001 392MAU 2002 271MAU 2003 271MAU 2004 273MAU 2005 273MAU	In Production 3Q02	EU 1Q03 NA 3Q02

Notes on table

- Bayer made a final decision on Wuppertal as the European manufacturing site in July 2000
- GI was only able to sell approximately 100 MAUs of Refacto® in 1999 therefore the actual capacity for Stockholm is given as less than 250 MAU
- Due to supply issues, Refacto® is not expected to be a significant player in the North American market until 2002
- Baxter Neuchatel capacity will be 750 MAU for old formulation and 1000MAU for protein-free formulation
- Launch dates for Recombinate® are the projected approval dates for the protein-free formulation

RECOMBINANT FACTOR VIII INTELLIGENCE REPORT

Major Events Timeline

Item	3Q00	4Q00	1Q01	2Q01	3Q01	4Q01	2002	2003	2004	2005
Bayer Berkeley Site full production							•			
Bayer Wuppertal full production										•
GI St Louis in full production							•			
GI Dublin in full production									•	
Baxter TO in full production		October 2000								
Baxter Neuchatel in full production								3Q03		
Kogenate FS® NA approval	June 2000									
Kogenate FS® EU approval	August 2000									
Kogenate FS® Japan approval			•	•	•	•				
Kogenate FS® Australia approval		•								

PROJECT BACKGROUND

Since the mid-1990s, the manufacturers of rFVIII products have taken initiatives to both improve the safety and increase the available global inventory of these products The result has been the introduction of new products with reduced amounts of human proteins and thus reducing the chance of viral infection such as took place in the late 1980s and early 1990s

Beyond the introduction of new and safer products, the industry has seen a significant increase in the planned manufacturing capacity for rFVIII products

Baxter Hyland Immuno's key new competitors in the rFVIII market are Bayer Corporation's Kogenate FS® and Genetic Institute's Refacto® It is therefore critical that Baxter Hyland Immuno's senior management be kept up to-date on the details surrounding these two products' timing of launch in various regional markets and the near-term supply of these products

The ultimate concern by Baxter is that as the global manufacturing capacity of rFVIII suppliers increases significantly over the next five years, the supply of rFVIII will ultimately outstrip demand This would create a new market dynamic in which rFVIII suppliers would find themselves in a competitive environment much more challenging than currently

OBJECTIVES

As a follow-up to the initial competitive intelligence report prepared for Baxter Hyland Immuno in June 2000, it was decided that the current and near-term (to 2005) manufacturing capacity figures should be verified and or updated

METHODOLOGY

Data Collection Richard Loomis conducted extensive data collection to garner all available public information on rFVIII manufacturing and distribution Data sources include commercial and public databases, Internet and published sources

Analysis Raw data was then analyzed by Mr Loomis and items of interest were followed up with primary (human source) research Findings from human source collection were then integrated with raw secondary data and analyzed for significance in terms of Baxter Hyland's intelligence needs

Report This report was then compiled utilizing secondary and primary source material as well as analysis conducted by Mr Loomis in cooperation with Baxter Hyland staff in marketing and operations Human source interview summaries are attached as an addendum to this report Copies of the secondary source material used in preparing this report are available on request Identities of human sources are concealed to protect these persons from potential embarrassment and to preserve them for future use

Ethics Mr Loomis operates within strict intelligence collection guidelines to ensure that Baxter Hyland Immuno does not incur legal or public relations liabilities that might stem from the use of unethical methods Mr Loomis intelligence collection methods are in keeping with the guidelines of the Society of Competitive Intelligence Professionals (SCIP) and are in compliance with a

federal and local statutes covering privacy and commercial proprietary information

BAYER CORPORATION KOGENATE FS®

CURRENT AND FUTURE MANUFACTURING CAPACITY

United States

Current Berkeley capacity

Estimating the current supply capacity of Berkeley has been complicated by conflicting information given by Bayer to the press and NHF As recently as September 2000 Bayer was telling the press that they could supply enough Kogenate FS for 70,000 patients [1] In November 2000 Bayer revised this estimate to NHF to be 140,000 patients [2] However, NHF estimates that Bayer supplies approximately 3000 patients with Kogenate and Kogenate FS Through an analysis of 1999 sales figures and applying certain reasonable assumptions, a current capacity figure is arrived at as follows

Assuming the following

- Bayer's total patient base is 3,000 [3]
- Bayer's on-demand patients represent 70 percent of this base [3]
- Kogenate sales for 1999 were approximately $401 3 million [4]

Approximate estimated supply of Kogenate in 1999 400 MAU

(See addendum for detailed figures)

In 1996 a Baxter internal memo reported that a Baxter scientist named R De Haven calculated Bayer's annual Kogenate capacity at their old facility (building 54) to be approximately 200 MAUs [5] In the same memo was a quote from a Bayer R&D official from a prepared statement to the U S Congress in 1995 that Bayer is investing several hundred million dollars at each of the multipurpose facilities

[1] New York Times, September 27, 2000
[2] Interview – Senior Staff, National Hemophilia Foundation
[3] Interview – Senior Marketing Staff, Baxter Hyland Immuno Europe
[4] MedAdNews , May 2000
[5] Internal memo, Baxter Hyland Immuno, June 12, 1996

(Clayton, NC and Berkeley, CA) to nearly double manufacturing capacity and support leading edge research and development activities" From this statement, Baxter personnel at the time estimated that the Berkeley facility could have an annual capacity of 500 MAUs of Kogenate

So, the estimates given by Baxter personnel in 1996 and an analysis of the sales figures done for 1999, both show a maximum capacity of approximately 500MAUs

Estimated future capacity of Berkeley, California facility

In 1996, Bayer began construction of a new Kogenate manufacturing facility on the Berkeley campus According to a review of engineering drawings of this plant conducted by Mr Loomis in June 2000, this new facility, building 60, is a 100 000 square foot plant with two bioreactor suites of six 200-liter bioreactors each for a total of twelve bioreactors plus two spare 200-liter bioreactors Building 60 was approved for production by the FDA in June-2000[6] (See June 2000 Intelligence Report for engineering drawings)

According to Baxter manufacturing personnel, the new technology being used by Bayer could yield up to ten times the capacity of an equivalent sized bioreactor at Baxter[7] This means that a single, 200-liter bioreactor at Berkeley could theoretically produce the same amount as a 2000-liter conventional bioreactor This translates into a theoretical maximum capacity for building 60 of 1000 MAUs per year (250 MAU per 3 bioreactors x 4 = 1000 MAU total)

In statements to the press and to the NHF, Bayer has indicated that they hope to double the capacity of the Berkeley facility by sometime in 2002[8][9] These statements,

[6] FDA approval letter to Bayer dated June 26, 2000 (FDA reference number 98-0656
[7] Interview - BDS Program Manager, Baxter Hyland Immuno
[8] Manufacturing Chemist, August 1999
[9] Interview – Senior Staff NHF, November 2000

combined with earlier capacity estimates and known details of Building 60 a[illegible] to an estimated total theoretical capacity of approximately 1000 MAUs per year by 2002

However, due to the lower yields of BHK cells (the source materia[illegible] for Kogenate FS® versus CHO cells (the source material for Recombinate®) the actual production capacity of Bayer's Berkeley facility is likely to be somewhat less than 1000 MAUs

From this information, a reasonable estimated potential capacity range for Bayer's Berkeley facility is approximately 750 MAUs per year This assumes that the difficulties involved in using BHK cells as a source material cause a 25% loss of efficiency in the bioreaction

Other Planned Berkeley expansion

In August 2000, Bayer announced that it was granted approval by the City of Berkeley to develop 14 additional acres just south of its present 34-acre site[1] Over the next five years, Bayer will spend approximately $120 million in constructing new facilities on the property

Plans for the site include

- A three-story, 100, 000 square foot warehouse/packaging facility
- A two-story, approximately 80,000 square foot Bulking and Sterile Fi[illegible] facility

Europe

Wuppertal, Germany

In April, 1999 Bayer Chairman Manfred Schneider said Bayer plans to build a second genetic engineering production site for its hemophilia medication Kogenate and rela

[10] Interview - Director of Operations, Baxter Hyland Immuno
[11] Bayer press release, August 9, 2000

the Wuppertal Germany site was high on the list [12] This was confirmed by a press report in July 2000 that indicated that Bayer had decided on building a Kogenate plant in Wuppertal and completing it by 2005 [13] Bayer does some Kogenate process development and also has a pilot plant at that location [14]

According to Baxter manufacturing managers, if Bayer keeps to a typical timeline for such a manufacturing facility, they should have the plant built and approved by sometime in 2005 if work begins in late 2000 or 1Q01 [15]

These estimates were recently confirmed when Bayer announced that they had decided to go forward with the Wuppertal project with a planned cost of $193 9 million[16] and an expected completion date of 2005 [17]

Regarding capacity of the Wuppertal facility, it is interesting to note that the early press report announcing the planned Wuppertal project stated that Bayer was planning to spend the equivalent of $146 million on building this manufacturing facility [17] This is almost precisely the same amount Baxter has budgeted for the Neuchatel facility Given this information, a rough estimate of the future capacity of Wuppertal would be approximately 750 MAU depending upon actual yield of the bioreactor suites

Wuppertal likely to be a Protein-free Kogenate facility

At a recent Bayer Kogenate Symposium in Europe, the Wuppertal plant plan was announced along with an announcement of Bayer plans for a 3rd generation (protein-free) product [18] This announcement, along with a 2005 completion date for

[12] AFX News April 28, 1999 Also reported in Chemical Business Newsbase May 5, 1999
[13] Chemical Week , July 19, 2000
[14] Interview - Investor Relations Manager, Bayer AG
[15] Interview – Operations staff, Baxter Hyland Immuno
[16] Chemical Week, November 8, 2000
[17] Chemical Week, July 19, 2000
[18] Interview – Senior Marketing staff, BaxterHyland Immuno, Europe, November 2000

Wuppertal, points to this facility being likely dedicated to production of a so-called 3rd generation product

PRODUCT LAUNCH DATES

United States and Canada

Kogenate FS® was approved in the U S in June 2000 [19]

Europe

Kogenate FS® was approved in the EU in August 2000 [20] Bayer launched the product in the UK in September 2000 [21] Bayer is expected to launch in the rest of the EU by the end of 2000

Japan and Asia

According to Bayer Corp sources in the U S, Kogenate FS® is expected to be approved in Japan sometime in 2001 [22] In the same conversation, the company indicated the expected launch approval date in Australia is 4Q00 Kogenate FS® was approved in New Zealand in 4Q99

[19] Med Ad News, August 2000
[20] Bayer press release, August 7, 2000
[21] Marketletter, September 11, 2000
[22] Interview – Director, Public Policy & Communications, Bayer Corp

PRICING STRATEGY

Bayer has positioned Kogenate FS® as a replacement for Kogenate and pricing in Europe to date has been identical to the old product [23,24] However, retail pricing in the U S of Kogerate FS® has been nearly 25% higher than that of other rFVIII products [25]

The confusion surrounding the pricing of Kogenate FS was clarified by NHF staff during an interview conducted in November 2000 [26] During this interview NHF indicated that although the average wholesale price (AWP) of Kogenate and Kogenate FS is identical at a $1 28 per unit, the PHS and non-PHS pricing is quite different It is summarized in the table below

Price scale	Kogenate	Kogenate FS
AWP	$1 28	$1 28
Non-PHS	$0 82	$1 13
PHS	$0 70	$0 96

[23] Internal memo, Baxter Hyland Immuno, October 6, 1999
[24] Interview – Senior Product Manager, Baxter Hyland Immuno
[25] National Hemophilia Foundation press release, September 26, 2000
[26] Interview – Senior NHF staff, November 2000

GENETICS INSTITUTE REFACTO®

CURRENT AND FUTURE MANUFACTURING CAPACITY

United States

St. Louis, MO

In August 1998, Genetics Institute purchased a biotech manufacturing fac- -n the town of Berkeley, Missouri near St Louis This is one of the o dest b otec- manufacturing facilities in the U S , having been originally bu- 'n the ear 1980s

Rumors that GI was having problems bringing this facility on-l ne na e beer widespread Delays could be due to equipment problems or s mp y d ffc es n bringing the plant into compliance with current FDA guidelines[27] Since the S- Louis facility was originally built, the guidelines for biotech manufacturing such as the U S Pharmacopoeia (currently USP 24 – NF 19 effecti e Jan ar 2 0 have been revised considerably The expense and effort required to upgrade an existing facility to these new standards can be extreme

Certainly given that Refacto® is already approved in the U S it can be assumed that GI had hoped to have an adequate supply of the produc a ailable for the North American market and be supplying that market through the U S p n

Also, the U S Refacto® approval included an indication for l m ted prophylactic administration of Refacto® Although physicians often administer rFVIII products prophylacticly for severe hemophilia on an off-label basis to go through the trouble to gain regulatory approval for such an indicat on h s that the manufacturer expected to have a considerable supply Th s s because

[27] Interview – Director of Operations, Baxter Hyland Immuno

prophylactic use of rFVIII requires a much greater supply than conventional use of the product [28]

In January 1999, an individual interviewing for a quality assurance position at the St. Louis facility was told that the plant was scheduled to be in consistency manufacturing in either 4Q99 or 1Q00 [29] This information correlates with company statements that the St Louis plant is scheduled to be in full production and approved by the FDA sometime in late 2001 [30] Further confirmation of a late 2001 or 2002 production date comes from the National Hemophilia Foundation Their sources in the field indicate that delays in St Louis are expected to push full production out to 2002 [31] For this reason, NHF believes that Refacto® will not have an impact on the U S market for two years despite the FDA approval of the product in March 2000

In October 2000, a senior NHF source stated that recently Genetics Institute had told NHF that they hoped to have the St Louis plant in full production sometime in calendar year 2002 [32] Despite continued rumors that GI is planning to abandon the St Louis plant, GI continues to indicate that the schedule for this facility is basically on schedule and due for production sometime in 2002

It is noteworthy that although the St Louis plant is scheduled to come on-line sometime in 2002, almost no published announcements have been made about this facility nor is it mentioned in any of American Home Products' recent SEC filings However, AHP has made extensive public statements regarding the construction of a biotech plant in Dublin, Ireland, which is not due to be completed until sometime in 2004

[28] Interview – Technical Marketing Manager, Baxter Hyland Immuno
[29] Interview – Director of Operations, Baxter Hyland Immuno
[30] Interview – VP North American Corporate Communications, American Home Products
[31] Interview – Director of Government Relations, NHF
[32] Interview – Director of Government Relations, NHF October 2000

Europe

Stockholm, Sweden

Currently, Refacto® is manufactured for Genetics Institute at the Pharmacia & Upjohn facility in Stockholm Sweden This plant is considered to have a maximum capacity of 250 MAUs However, in 1999 GI only sold approximately 100 MAUs of Refacto in the EU Further hints of production problems in Stockholm were indicated during a February 2000 meeting between Baxter marketing managers and American Home Products' European marketing personnel During this meeting the AHP executives indicated frustration regarding supply issues surrounding both Benefix and Refacto[33]

Dublin, Ireland

In early April 2000 American Home Products announced plans to invest approximately $685 million to expand its Wyeth Medica Ireland manufacturing operations by building a new biotechnology facility at The Grange Castle in South Dublin County, Ireland The products planned to be manufactured at the expanded Ireland facility include "Antihaemophilic Factor VIII for patients with Haemophilia A formulated in the absence of Human Serum Albumin"[34] In the same announcement AHP indicated that the company planned to begin construction on this site in the Fall of 2000 and be operational sometime in 2004 Contacts at Genetics Institute in the United States indicated that construction of the plant in Ireland would not impact the company's plans for St Louis[35] This source went on to state that the company intended that Stockholm would continue to supply Refacto® to the EU and US (in small quantities) until St Louis was operational St Louis would supply the North American market, and Ireland would supply Refacto® globally

Capacity in Dublin

Calculations for Refacto capacity is currently impossible for two reasons first, very little is known about the planned facility, and second, the facility will not be dedicated

[33] Interview – Director of Coagulation Products, Europe, Baxter Hyland Immuno
[34] AHP press release, April 4, 2000
[35] Interview – VP North American Corporate Communications, American Home Products

to exclusive production of Refacto Besides Refacto, the Dublin facility is planned to produce three other products, Prevnar, Enbrel, and BMP2 [36]

PRODUCT LAUNCH DATES

United States and Canada

The U S FDA approved Refacto® in early March 2000 [37] However, due to supply problems and delays in getting their St Louis plant on-line, Refacto® is not expected to be a major player in the North American market until 2002 The company had indicated that small amounts of the product were planned to be diverted from Europe by September 2000 [38] As of November 2000, GI informed NHF that they will not even begin to market Refacto® until early 2001 [39]

Europe

Refacto® was approved in the EU in 2Q99 Since this approval, Refacto® has been able to sell to between 6 and 7% of the EU market According to Baxter sources in Europe, much of this initial success can be traced to shortages of old formulation Kogenate® in Europe in 1999 [40]

[36] Chemical Market Reporter, April 10, 2000
[37] AHP Press release, March 7, 2000
[38] Interview – Director of Government Relations, NHF
[39] NHF Medical Advisory #371, September 11, 2000
[40] Interview – Senior Marketing Analyst, Global Marketing, Baxter Hyland Immuno

Japan and Asia

According to an AHP source in the U S , the regulatory filing for Refacto® in Japan is being handled by Yamanouchi Pharmaceuticals[41] The source did not know the projected approval date for Japan The source did indicate that the company has no current schedule for gaining approval of Refacto® in Australia or New Zealand

[41] Interview – VP International Corporate Communications, American Home Products

OTHER SUPPLY RELATED ISSUES

BAYER DIRECT[SM]

In September 2000, Bayer announced that Kogenate FS® would be distributed in the U S through a direct distribution program called Bayer Direct[SM] Bayer claims that this program is designed to maintain a reliable supply to patients at consistent pricing similar to first-generation rFVIII products[42] However, this program has proven to be very controversial and extremely unpopular with NHF According to a senior NHF executive, Bayer informed NHF of Bayer Direct[SM] on Thursday August 31, 2000 and launched the program the following Tuesday, September 5, 2000[43] This source indicated that there remains "a wide chasm" between Bayer and NHF regarding the ethics of implementing such a distribution program In fact, on September 25, 2000, the same day as the official launch of Bayer Direct[SM], NHF announced that it was renouncing all corporate support from Bayer in protest over Bayer Direct[SM][44] NHF accused Bayer of attempting to profiteer through this distribution scheme noting that patients would be restricted to only one source for Kogenate FS with a price set at the non-PHS rate

As a result of the BayerDirect controversy, Bayer has now indicated that they will continue to supply Kogenate to hospitals, clinics and home health care companies[45] As of this report going to print, NHF had not had direct talks with Bayer regarding this new policy

[42] Bayer press release, September 26, 2000
[43] Interview – NHF staff, October 2000
[44] NHF press release, September 26, 2000
[45] New York Times, November 11, 2000

Interestingly, Bayer had originally planned to enroll approximately 700 patients in BayerDirect for Kogenate FS However, as of this report going to print, NHF indicates that only 70 patients have signed up for the program [46]

PROJECTED KOGENATE FS® SUPPLY 2002 & 2003

An estimate of Kogenate FS® sales for 2002 is $518 million.[47] This translates into a projected supply of Kogenate FS® for 2002 of approximately 508 MAU

An estimate of Kogenate FS® sales for 2003 is $700 million [48] This translates into a projected supply of Kogenate FS® for 2003 of approximately 686 MAU

(Note These calculations based on a per unit net price of $1 02 See addendum

[46] Interview – Senior NHF staff, November 2000
[47] MedAdNews, May 2000
[48] Chemical Week, July 19, 2000

ADDENDUM: BAYER RFVIII SUPPLY MODEL FOR YEAR 1999

Addendum
Bayer rFVIII Supply Model for Year 1999

On Demand rFVIII patient model	
Total estimated Bayer patients	3,000
Total est Bayer on demand patients	2,100
Average patient weight (kg)	77
Average dose per kg weight	50
Average units per year per patient	45,900
Total annual est Bayer on demand units	**96,390,000**
Prophylactic rFVIII patient model	
Total estimated Bayer patients	3,000
Total est Bayer prophylactic patients	900
Average patient weight (kg)	77
Average dose per kg weight	30
Average units per year per patient	330,480
Total annual est Bayer prophylactic units	**297,432,000**
Total annual est Bayer rFVIII supply	**393,822,000**
Average realized price per unit	**$1 02**

Note Average realized price per unit based on 1999 Kogenate sales of $403 4 million

NOTE

Prepard by Richard Loomis 11/22/00
Confidential

NOTE

Index of Interviews

Senior Staff, National Hemophilia Foundation, Washington, DC

Interview: BHI2-1

Title: Senior Staff

Organization: National Hemophilia Foundation, Washington. DC

Background.

This contact has direct access to information regarding projected supplies of rFVIII products in the U S This contact frequently meets with senior management of rFVIII suppliers to discuss issues surrounding the supply of rFVIII products

Source Comments:

The source was questioned about NHF's current information on rFVIII manufacturing capacity

Regarding GI's Refacto plant in St Louis, the source indicated that the last word GI had given NHF was that this facility is scheduled to be in full production sometime in calendar year 2002 NHF was not aware that the American Home Products plant being built in Ireland is also planned to produce Refacto beginning in 2004 GI's supply of Refacto from Stockholm continues to be limited and NHF indicates that the company is not taking on any new customers for the time being as a result

Regarding Kogenate FS, the contact was not sure about the timing of Berkeley's planning of going into full production The source stated that NHF's understanding was that Bayer was still waiting on approval of a 200 liter fermenter NHF was not aware of Bayer's plans to build a European Kogenate manufacturing facility in Wuppertal Germany

The contact went on to discuss some background on NHF s position on Bayer Direct According to the source, Bayer notified NHF on Thursday August 31 2000 that Bayer Direct would be launched the following Tuesday, September 5, 2000 NHF had no prior

warning from Bayer regarding this program When asked if NHF had made any progress in persuading Bayer to modify the Bayer Direct program, the source stated that there remained "a wide chasm of disagreement" between the two parties

Analyst Comments

Bayer was granted approval of the Kogenate FS production in building 60 in an approval letter from the FDA dated June 26, 2000 The reference the source makes to Bayer awaiting approval of a 200 liter fermenter may be in error The analyst suspects that Bayer was actually telling NHF that they were awaiting approval of the entire production facility in building 60 Building 60 is made up of twelve 200 liter bioreactors (plus two spare 200 liter reactors) utilizing a new process technology that is significantly different from what Bayer had used in the past in producing Kogenate This will be verified in a future interview with this contact

Senior Operations Staff, Baxter Hyland Immuno

Interview: BHI2-2

Title: Senior Staff

Organization: Baxter Hyland Immuno

Background:

This source has a large network of contacts within the biotech industry and was contacted for an update on competitive capacity as well as information regarding the latest timelines for Baxter's rFVIII production facilities

Source comments

The source said that he had heard that Bayer's Berkeley plant had lost a lot of Kogenate FS due to mold problems

When asked about Bayer's plans for Wuppertal, the source indicated that if Bayer stuck to a fairly standard timeline they should be approved and capable of full production in 2005 This assumes 6 months to plan, 2 years to build, and 2 years to validate and approve the facility

Given that Bayer's stated capital outlay for Wuppertal is similar to Baxter's for Neuchatel, the source estimated that Wuppertal will have a capacity of between 750-1000 MAUs per year

Regarding Genetics Institute, the source stated that he is still hearing rumors that GI is planning to abandon the St Louis plant He noted that GI is building a new 220 000 square foot facility at its Andover Maryland campus However, the source was uncertain of this facility's purpose

Regarding the status of Baxter's Neuchatel plant, the source sta ed that live cell cultures were to be run in November 2000 and conformance lots were planned for December 2000 or January 2001 In Thousand Oaks, suite B had received FDA approval and has already run 7 campaigns Thousand Oaks' suite C has run 5 campaigns anc is hoping to gain FDA approval within two weeks

The interview concluded with the source providing updated con act information for other Baxter operations staff personnel

Analyst comments:

The Kogenate FS lot referred to be the source may be either lo 670H076 or 670H071C which were voluntarily withdrawn by Bayer in late August 2000 due to low potency

Senior Marketing Staff, Baxter Hyland Immuno

Interview: BHI2-3

Title: Senior Marketing Staff

Organization: Baxter Hyland Immuno

Background:

This source has access to competitive pricing information from the field sales force [illegible] this source is knowledgeable regarding the typical dosing regimens for hemophiliac patients

Source comments

The source provided the following pricing information for Kogenate FS

Pricing category	*Cost per unit*
Average Wholesale Price	$1 28
Direct-to-Patient	$1 13
PHS	$0 99

The conversation then turned to the typical dosing regimens for hemophiliacs being treated with rFVIII The source indicated that on-demand patients typically use rFVIII once per month at a dosage of 50 units/kg In the case of prophylactic patients the dosage regimen is typically 25-40 units/kg

Analyst comments

The PHS pricing for Kogenate FS has been recently reduced (according to NHF sources) to 96 cents per unit

The dosage regimen information and pricing was used by the analyst to construct a supply model for Kogenate FS using dollar sales projections supplied by Bayer This is to be included in the final report of this project as an addendum

Senior Staff, National Hemophilia Foundation, Washington, DC

Interview: BHI2-4

Title: Senior Staff

Organization: National Hemophilia Foundation, Washington, DC

Background:

This source was contacted a second time for this project to clarify issues surrounding the pricing structure of Kogenate FS Press releases by NHF had indicated that Kogenate FS was being sold at a 25% premium over the old formulation Countering this has been repeated statements by Bayer that Kogenate FS is priced at the same level as the old formulation

Source comments:

When asked to clarify the discrepancy between statements by NHF and Bayer regarding Kogenate FS pricing, the source indicated that the average wholesale price (AWP) for Kogenate and Kogenate FS was indeed, identical This is why Bayer can claim that Kogenate FS is at the same price level as the old formulation However AWP is a somewhat arbitrary number, in that it does not reflect actual retail pricing of the product. Additionally, although the AWP is supposedly a wholesale price, the actual retail pricing of the product is less than AWP The NHF source summarized the Kogenate and Kogenate FS pricing structure as follows

Pricing category	*Kogenate (old formula)*	*Kogenate FS*
AWP	$1 28	$1 28
Non-PHS	$0 82	$1 13
PHS	$0 70	$0 96

The source pointed out that in the Bayer Direct distribution scheme patients would be charged at the non-PHS price level of $1 13 per unit versus the old non-PHS price level of $0 82 per unit In addition, Bayer is attempting to distribute Kogenate FS exclusively through Bayer Direct, which would translate into many more patients at the non-PHS price level

Finally, the source was asked the number of patients that NHF estimates Bayer serves with Kogenate each year The source indicated that although Bayer has given patient numbers ranging from 700-1700 patients, NHF estimates that Bayer actually has 3000 patients using Kogenate or Kogenate FS

The analyst brought up Bayer statements that they hope to enroll approximately 700 patients in Bayer Direct The source indicated that due to the negative publicity surrounding the Bayer Direct program, Bayer has only been able to enroll 70 patients in Bayer Direct as of late October 2000

Finally, the source was asked about NHF's information regarding the approval of Bayer's expansion suite in Berkeley The source indicated that the last word Bayer had given NHF, was that they were awaiting FDA approval of a new 200 liter bioreactor in Berkeley The analyst asked the source if it was possible that Bayer was awaiting approval on a *type of 200 liter reactor, not just a single, 200 liter unit* In other words, could it be possible that Bayer was actually awaiting approval for a group of 200 liter bioreactors? The source stated that this it was definitely possible that he had been mistaken in assuming that Bayer was only waiting approval of one, 200 liter bioreactor The source stated that he was not familiar with the details of the manufacturing facility in Berkeley and this could have caused him to make an incorrect assumption

Analyst comments:

The new PHS pricing level of $0 96 is slightly lower than Baxter's last information. [illegible] placed this at $0 99 per unit.

The information on estimated number of patients that Bayer has using Kogenate and Kogenate FS will be used in the rFVIII supply model addendum to the final report of this project

Re FVIII - Global

Mfg Capacity

Update

RECOMBINANT FACTOR VIII GLOBAL MANUFACTURING CAPACITY UPDATE NOVEMBER 2000

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RECOMBINANT FACTOR VIII GLOBAL MANUFACTURING CAPACITY

EXECUTIVE SUMMARY

This research was conducted in late October 2000 verify and update rFVIII manufacturing capacity estimates contained in a previous competitive intelligence report prepared in June 2000 for Baxter Hyland Immuno The objective of this follow-up research was to estimate the current and potential manufacturing capacity for Bayer's Kogenate FS® and Genetics Institute's Refacto®

KEY FINDINGS

The key findings of this research are summarized in the table below

Product	Manufacturing Sites and Capacity	Date of Full Production	Launch Dates
Kogenate FS®	Berkeley, CA <500 MAU Expanded capacity <500 MAU Wuppertal, Germany 750 MAU	In production 2002 2005	EU 4Q00 NA 4Q01 Japan 2H.. Austra..a 4Q0. NZ Launched
Refacto®	Stockholm,Sweden <250MAU St Louis, MO Unknown Dublin, Ireland Unknown	In production 2002 2004	EU Launched NA March 2001 effective 4Q.. Japar Yamanouchi filing Austra..a No scheduled NZ No scheduled
Recombinate®	Thousand Oaks, CA 750-825MAU Neuchatel,Swit 750-1000MAU On contract from GI 2000 380MAU 2001 392MAU 2002 271MAU 2003 271MAU 2004 273MAU 2005 273MAU	In Production 3Q02	EU 1Q03 NA 3Q02

Notes on table

- Bayer made a final decision on Wuppertal as the European manufacturing site in July 2000
- GI was only able to sell approximately 100 MAUs of Refacto® in 1999 therefore the actual capacity for Stockholm is given as less than 250 MAU
- Due to supply issues, Refacto® is not expected to be a significant player in the North American market until 2002
- Baxter Neuchatel capacity will be 750 MAU for old formulation and 1000MAU for protein-free formulation
- Launch dates for Recombinate® are the projected approval dates for the protein-free formulation

RECOMBINANT FACTOR VIII INTELLIGENCE REPORT

Major Events Timeline

Item	3Q00	4Q00	1Q01	2Q01	3Q01	4Q01	2002	2003	2004	2005
Bayer Berkeley Site full production							•			
Bayer Wuppertal full production										•
GI St Louis in full production							•			
GI Dublin in full production									•	
Baxter TO in full production		October 2000								
Baxter Neuchatel in full production								3Q03		
Kogenate FS® NA approval	June 2000									
Kogenate FS® EU approval	August 2000									
Kogenate FS® Japan approval			•	•	•	•				
Kogenate FS® Australia approval		•								

PROJECT BACKGROUND

Since the mid-1990s, the manufacturers of rFVIII products have taken initiatives to both improve the safety and increase the available global inventory of these products The result has been the introduction of new products with reduced amounts of human proteins and thus reducing the chance of viral infection such as took place in the late 1980s and early 1990s

Beyond the introduction of new and safer products, the industry has seen a significant increase in the planned manufacturing capacity for rFVIII products

Baxter Hyland Immuno's key new competitors in the rFVIII market are Bayer Corporation's Kogenate FS® and Genetic Institute's Refacto® It is therefore critical that Baxter Hyland Immuno's senior management be kept up to-date on the details surrounding these two products' timing of launch in various regional markets and the near-term supply of these products

The ultimate concern by Baxter is that as the global manufacturing capacity of rFVIII suppliers increases significantly over the next five years, the supply of rFVIII will ultimately outstrip demand This would create a new market dynamic in which rFVIII suppliers would find themselves in a competitive environment much more challenging than currently

OBJECTIVES

As a follow-up to the initial competitive intelligence report prepared for Baxter Hyland Immuno in June 2000, it was decided that the current and near-term (to 2005) manufacturing capacity figures should be verified and or updated

METHODOLOGY

Data Collection Richard Loomis conducted extensive data collection to gather all available public information on rFVIII manufacturing and distribution Data sources include commercial and public databases, Internet and published sources

Analysis Raw data was then analyzed by Mr Loomis and items of interest were followed up with primary (human source) research Findings from human source collection were then integrated with raw secondary data and analyzed for significance in terms of Baxter Hyland's intelligence needs

Report This report was then compiled utilizing secondary and primary source material as well as analysis conducted by Mr Loomis in cooperation with Baxter Hyland staff in marketing and operations Human source interview summaries are attached as an addendum to this report Copies of the secondary source material used in preparing this report are available on request Identities of human sources are concealed to protect these persons from potential embarrassment and to preserve them for future use

Ethics Mr Loomis operates within strict intelligence collection guidelines to ensure that Baxter Hyland Immuno does not incur legal or public relations liabilities that might stem from the use of unethical methods Mr Loomis intelligence collection methods are in keeping with the guidelines of the Society of Competitive Intelligence Professionals (SCIP) and are in compliance with a

federal and local statutes covering privacy and commercial proprietary information

BAYER CORPORATION KOGENATE FS®

CURRENT AND FUTURE MANUFACTURING CAPACITY

United States

Current Berkeley capacity

Estimating the current supply capacity of Berkeley has been complicated by conflicting information given by Bayer to the press and NHF As recently as September 2000 Bayer was telling the press that they could supply enough Kogenate FS for 3000 patients [1] In November 2000 Bayer revised this estimate to NHF to be 1 700 patients [2] However, NHF estimates that Bayer supplies approximately 3000 patients with Kogenate and Kogenate FS Through an analysis of 1999 sales figures and applying certain reasonable assumptions, a current capacity figure is arrived at as follows

Assuming the following

- Bayer's total patient base is 3,000 [2]
- Bayer's on-demand patients represent 70 percent of this base [3]
- Kogenate sales for 1999 were approximately $401 3 million [4]

Approximate estimated supply of Kogenate in 1999 400 MAU

(See addendum for detailed figures)

In 1996 a Baxter internal memo reported that a Baxter scientist named R De[illegible]er calculated Bayer's annual Kogenate capacity at their old facility (building 5[illegible] to be approximately 200 MAUs [5] In the same memo was a quote from a Bayer R&D official from a prepared statement to the U S Congress in 1995 that Bayer is investing several hundred million dollars at each of the multipurpose facilities

[1] New York Times, September 27, 2000
[2] Interview – Senior Staff, National Hemophilia Foundation
[3] Interview – Senior Marketing Staff, Baxter Hyland Immuno Europe
[4] MedAdNews , May 2000
[5] Internal memo, Baxter Hyland Immuno, June 12, 1996

(Clayton, NC and Berkeley, CA) to nearly double manufacturing capacity and support leading edge research and development activities" From this statement, Baxter personnel at the time estimated that the Berkeley facility could have an annual capacity of 500 MAUs of Kogenate

So, the estimates given by Baxter personnel in 1996 and an analysis of the sales figures done for 1999, both show a maximum capacity of approximately 500MAUs

Estimated future capacity of Berkeley, California facility

In 1996, Bayer began construction of a new Kogenate manufacturing facility on the Berkeley campus According to a review of engineering drawings of this plant conducted by Mr Loomis in June 2000, this new facility, building 60, is a 100 000 square foot plant with two bioreactor suites of six 200-liter bioreactors each for a total of twelve bioreactors plus two spare 200-liter bioreactors Building 60 was approved for production by the FDA in June-2000[6] (See June 2000 Intelligence Report for engineering drawings)

According to Baxter manufacturing personnel, the new technology being used by Bayer could yield up to ten times the capacity of an equivalent sized bioreactor at Baxter[7] This means that a single, 200-liter bioreactor at Berkeley could theoretically produce the same amount as a 2000-liter conventional bioreactor This translates into a theoretical maximum capacity for building 60 of 1000 MAUs per year (250 MAU per 3 bioreactors x 4 = 1000 MAU total)

In statements to the press and to the NHF, Bayer has indicated that they hope to double the capacity of the Berkeley facility by sometime in '002[8][9] These statements,

[6] FDA approval letter to Bayer dated June 26, 2000 (FDA reference number 98-0656
[7] Interview - BDS Program Manager, Baxter Hyland Immuno
[8] Manufacturing Chemist, August 1999
[9] Interview – Senior Staff NHF, November 2000

combined with earlier capacity estimates and known details of Building 60 a[illegible] point to an estimated total theoretical capacity of approximately 1000 MAUs per year by 2002

However, due to the lower yields of BHK cells (the source materia[illegible] for Kogenate FS® versus CHO cells (the source material for Recombinate®) the actual production capacity of Bayer's Berkeley facility is likely to be somewhat less than 1000 MAUs

From this information, a reasonable estimated potential capacity range for Bayer's Berkeley facility is approximately 750 MAUs per year This assumes that the difficulties involved in using BHK cells as a source material cause a 25% loss of efficiency in the bioreaction

Other Planned Berkeley expansion

In August 2000, Bayer announced that it was granted approval by the City of Berkeley to develop 14 additional acres just south of its present 34-acre site[1] Over the next five years, Bayer will spend approximately $120 million in constructing new facilities on the property

Plans for the site include

- A three-story, 100, 000 square foot warehouse/packaging facility
- A two-story, approximately 80,000 square foot Bulking and Sterile Fi[illegible] facility

Europe

Wuppertal, Germany

In April, 1999 Bayer Chairman Manfred Schneider said Bayer plans to build a second genetic engineering production site for its hemophilia medication Kogenate and tha[illegible]

[10] Interview - Director of Operations, Baxter Hyland Immuno

[11] Bayer press release, August 9, 2000

the Wuppertal Germany site was high on the list [12] This was confirmed by a press report in July 2000 that indicated that Bayer had decided on building a Kogenate plant in Wuppertal and completing it by 2005 [13] Bayer does some Kogenate process development and also has a pilot plant at that location [14]

According to Baxter manufacturing managers, if Bayer keeps to a typical timeline for such a manufacturing facility, they should have the plant built and approved by sometime in 2005 if work begins in late 2000 or 1Q01 [15]

These estimates were recently confirmed when Bayer announced that they had decided to go forward with the Wuppertal project with a planned cost of $193 9 million[16] and an expected completion date of 2005 [17]

Regarding capacity of the Wuppertal facility, it is interesting to note that the early press report announcing the planned Wuppertal project stated that Bayer was planning to spend the equivalent of $146 million on building this manufacturing facility [17] This is almost precisely the same amount Baxter has budgeted for the Neuchatel facility Given this information, a rough estimate of the future capacity of Wuppertal would be approximately 750 MAU depending upon actual yield of the bioreactor suites

Wuppertal likely to be a Protein-free Kogenate facility

At a recent Bayer Kogenate Symposium in Europe, the Wuppertal plant plan was announced along with an announcement of Bayer plans for a 3rd generation (protein-free) product [18] This announcement, along with a 2005 completion date for

[12] AFX News April 28, 1999 Also reported in Chemical Business Newsbase May 5, 1999
[13] Chemical Week , July 19, 2000
[14] Interview - Investor Relations Manager, Bayer AG
[15] Interview – Operations staff, Baxter Hyland Immuno
[16] Chemical Week, November 8, 2000
[17] Chemical Week, July 19, 2000
[18] Interview – Senior Marketing staff, Baxter Hyland Immuno, Europe, November 2000

Wuppertal, points to this facility being likely dedicated to production of a so-called 3rd generation product

PRODUCT LAUNCH DATES

United States and Canada

Kogenate FS® was approved in the U S in June 2000 [19]

Europe

Kogenate FS® was approved in the EU in August 2000 [20] Bayer launched the product in the UK in September 2000 [21] Bayer is expected to launch in the rest of the EU by the end of 2000

Japan and Asia

According to Bayer Corp sources in the U S, Kogenate FS® is expected to be approved in Japan sometime in 2001 [22] In the same conversation, the company indicated the expected launch approval date in Australia is 4Q00 Kogenate FS® was approved in New Zealand in 4Q99

[19] Med Ad News, August 2000
[20] Bayer press release, August 7, 2000
[21] Marketletter, September 11, 2000
[22] Interview – Director, Public Policy & Communications, Bayer Corp

PRICING STRATEGY

Bayer has positioned Kogenate FS® as a replacement for Kogenate and pricing in Europe to date has been identical to the old product [23,24] However, retail pricing in the U S of Kogerate FS® has been nearly 25% higher than that of other rFVIII products [25]

The confusion surrounding the pricing of Kogenate FS was clarified by NHF staff during an interview conducted in November 2000 [26] During this interview NHF indicated that although the average wholesale price (AWP) of Kogenate and Kogenate FS is identical at a $1 28 per unit, the PHS and non-PHS pricing is quite different It is summarized in the table below

Price scale	Kogenate	Kogenate FS
AWP	$1 28	$1 28
Non-PHS	$0 82	$1 13
PHS	$0 70	$0 96

[23] Internal memo, Baxter Hyland Immuno, October 6, 1999
[24] Interview – Senior Product Manager, Baxter Hyland Immuno
[25] National Hemophilia Foundation press release, September 26, 2000
[26] Interview – Senior NHF staff, November 2000

GENETICS INSTITUTE REFACTO®

CURRENT AND FUTURE MANUFACTURING CAPACITY

United States

St. Louis, MO

In August 1998, Genetics Institute purchased a biotech manufacturing facility in the town of Berkeley, Missouri near St Louis This is one of the oldest biotech manufacturing facilities in the U S , having been originally built in the early 1980s

Rumors that GI was having problems bringing this facility on-line have been widespread Delays could be due to equipment problems or simply difficulties in bringing the plant into compliance with current FDA guidelines[27] Since the St Louis facility was originally built, the guidelines for biotech manufacturing such as the U S Pharmacopoeia (currently USP 24 – NF 19 effective January 2000) have been revised considerably The expense and effort required to upgrade an existing facility to these new standards can be extreme

Certainly given that Refacto® is already approved in the U S it can be assumed that GI had hoped to have an adequate supply of the product available for the North American market and be supplying that market through the U S plant

Also, the U S Refacto® approval included an indication for limited prophylactic administration of Refacto® Although physicians often administer rFVIII products prophylacticly for severe hemophilia on an off-label basis to go through the trouble to gain regulatory approval for such an indication hints that the manufacturer expected to have a considerable supply This is because

[27] Interview – Director of Operations, Baxter Hyland Immuno

prophylactic use of rFVIII requires a much greater supply than conventional use of the product [28]

In January 1999, an individual interviewing for a quality assurance position at the St. Louis facility was told that the plant was scheduled to be in consistency manufacturing in either 4Q99 or 1Q00 [29] This information correlates with company statements that the St Louis plant is scheduled to be in full production and approved by the FDA sometime in late 2001 [30] Further confirmation of a late 2001 or 2002 production date comes from the National Hemophilia Foundation Their sources in the field indicate that delays in St Louis are expected to push full production out to 2002 [31] For this reason, NHF believes that Refacto® will not have an impact on the U S market for two years despite the FDA approval of the product in March 2000

In October 2000, a senior NHF source stated that recently Genetics Institute had told NHF that they hoped to have the St Louis plant in full production sometime in calendar year 2002 [32] Despite continued rumors that GI is planning to abandon the St Louis plant, GI continues to indicate that the schedule for this facility is basically on schedule and due for production sometime in 2002

It is noteworthy that although the St Louis plant is scheduled to come on-line sometime in 2002, almost no published announcements have been made about this facility nor is it mentioned in any of American Home Products' recent SEC filings However, AHP has made extensive public statements regarding the construction of a biotech plant in Dublin, Ireland, which is not due to be completed until sometime in 2004

[28] Interview – Technical Marketing Manager, Baxter Hyland Immuno
[29] Interview – Director of Operations, Baxter Hyland Immuno
[30] Interview – VP North American Corporate Communications, American Home Products
[31] Interview – Director of Government Relations, NHF
[32] Interview – Director of Government Relations, NHF October 2000

Europe

Stockholm, Sweden

Currently, Refacto® is manufactured for Genetics Institute at the Pharmacia & Upjohn facility in Stockholm Sweden This plant is considered to have a maximum capacity of 250 MAUs However, in 1999 GI only sold approximately 100 MAUs of Refacto in the EU Further hints of production problems in Stockholm were indicated during a February 2000 meeting between Baxter marketing managers and American Home Products' European marketing personnel During this meeting the AHP executives indicated frustration regarding supply issues surrounding both Benefix and Refacto

Dublin, Ireland

In early April 2000 American Home Products announced plans to invest approximately $685 million to expand its Wyeth Medica Ireland manufacturing operations by building a new biotechnology facility at The Grange Castle in South Dublin County, Ireland The products planned to be manufactured at the expanded Ireland facility include "Antihaemophilic Factor VIII for patients with Haemophilia A formulated in the absence of Human Serum Albumin "[34] In the same announcement AHP indicated that the company planned to begin construction on this site in the Fall of 2000 and be operational sometime in 2004 Contacts at Genetics Institute in the United States indicated that construction of the plant in Ireland would not impair the company's plans for St Louis[35] This source went on to state that the company intended that Stockholm would continue to supply Refacto® to the EU and U S in small quantities) until St Louis was operational St Louis would supply the North American market, and Ireland would supply Refacto® globally

Capacity in Dublin

Calculations for Refacto capacity is currently impossible for two reasons first, very little is known about the planned facility, and second, the facility will not be dedicated

[33] Interview – Director of Coagulation Products, Europe, Baxter Hyland Immuno

[34] AHP press release, April 4, 2000

[35] Interview – VP North American Corporate Communications, American Home Products

to exclusive production of Refacto Besides Refacto, the Dublin facility is planned to produce three other products, Prevnar, Enbrel, and BMP2 [36]

PRODUCT LAUNCH DATES

United States and Canada

The U S FDA approved Refacto® in early March 2000 [37] However, due to supply problems and delays in getting their St Louis plant on-line, Refacto® is not expected to be a major player in the North American market until 2002 The company had indicated that small amounts of the product were planned to be diverted from Europe by September 2000 [38] As of November 2000, GI informed NHF that they will not even begin to market Refacto® until early 2001 [39]

Europe

Refacto® was approved in the EU in 2Q99 Since this approval, Refacto® has been able to sell to between 6 and 7% of the EU market According to Baxter sources in Europe, much of this initial success can be traced to shortages of old formulation Kogenate® in Europe in 1999 [40]

[36] Chemical Market Reporter, April 10, 2000
[37] AHP Press release, March 7, 2000
[38] Interview – Director of Government Relations, NHF
[39] NHF Medical Advisory #371, September 11, 2000
[40] Interview – Senior Marketing Analyst, Global Marketing, Baxter Hyland Immuno

Japan and Asia

According to an AHP source in the U S , the regulatory filing for Refacto® in Japan is being handled by Yamanouchi Pharmaceuticals[41] The source did not know the projected approval date for Japan The source did indicate that the company has no current schedule for gaining approval of Refacto® in Australia or New Zealand

[41] Interview – VP International Corporate Communications, American Home Products

OTHER SUPPLY RELATED ISSUES

BAYER DIRECT[SM]

In September 2000, Bayer announced that Kogenate FS® would be distributed in the U S through a direct distribution program called Bayer Direct[SM] Bayer claims that this program is designed to maintain a reliable supply to patients at consistent pricing similar to first-generation rFVIII products[42] However, this program has proven to be very controversial and extremely unpopular with NHF According to a senior NHF executive, Bayer informed NHF of Bayer Direct[SM] on Thursday August 31, 2000 and launched the program the following Tuesday, September 5, 2000[43] This source indicated that there remains "a wide chasm" between Bayer and NHF regarding the ethics of implementing such a distribution program In fact, on September 25, 2000, the same day as the official launch of Bayer Direct[SM], NHF announced that it was renouncing all corporate support from Bayer in protest over Bayer Direct[SM][44] NHF accused Bayer of attempting to profiteer through this distribution scheme noting that patients would be restricted to only one source for Kogenate FS with a price set at the non-PHS rate

As a result of the BayerDirect controversy, Bayer has now indicated that they will continue to supply Kogenate to hospitals, clinics and home health care companies[45] As of this report going to print, NHF had not had direct talks with Bayer regarding this new policy

[42] Bayer press release, September 26, 2000
[43] Interview – NHF staff, October 2000
[44] NHF press release, September 26, 2000
[45] New York Times, November 11, 2000

Interestingly, Bayer had originally planned to enroll approximately 700 patients in BayerDirect for Kogenate FS However, as of this report going to print, NHF indicates that only 70 patients have signed up for the program [46]

PROJECTED KOGENATE FS® SUPPLY 2002 & 2003

An estimate of Kogenate FS® sales for 2002 is $518 million.[47] This translates into a projected supply of Kogenate FS® for 2002 of approximately 508 MAU

An estimate of Kogenate FS® sales for 2003 is $700 million [48] This translates into a projected supply of Kogenate FS® for 2003 of approximately 686 MAU

(Note These calculations based on a per unit net price of $1 02 See addendum

[46] Interview – Senior NHF staff, November 2000
[47] MedAdNews, May 2000
[48] Chemical Week, July 19, 2000

ADDENDUM: BAYER RFVIII SUPPLY MODEL FOR YEAR 1999

Addendum
Bayer rFVIII Supply Model for Year 1999

On Demand rFVIII patient model	
Total estimated Bayer patients	3,000
Total est Bayer on demand patients	2,100
Average patient weight (kg)	77
Average dose per kg weight	50
Average units per year per patient	45,900
Total annual est Bayer on demand units	**96,390,000**
Prophylactic rFVIII patient model	
Total estimated Bayer patients	3,000
Total est Bayer prophylactic patients	900
Average patient weight (kg)	77
Average dose per kg weight	30
Average units per year per patient	330,480
Total annual est Bayer prophylactic units	**297,432,000**
Total annual est Bayer rFVIII supply	**393,822,000**
Average realized price per unit	**$1 02**

Note Average realized price per unit based on 1999 Kogenate sales of $403 4 million

NOTE

Prepard by Richard Loomis 11/22/00
Confidential

NOTE

Index of Interviews

Senior Staff, National Hemophilia Foundation, Washington, DC

Interview: BHI2-1

Title: Senior Staff

Organization: National Hemophilia Foundation, Washington, DC

Background.

This contact has direct access to information regarding projected supplies of rFVIII products in the U S This contact frequently meets with senior management of rFVIII suppliers to discuss issues surrounding the supply of rFVIII products

Source Comments:

The source was questioned about NHF's current information on rFVIII manufacturing capacity

Regarding GI's Refacto plant in St Louis, the source indicated that the last word GI had given NHF was that this facility is scheduled to be in full production sometime in calendar year 2002 NHF was not aware that the American Home Products plant being built in Ireland is also planned to produce Refacto beginning in 2004 GI's supply of Refacto from Stockholm continues to be limited and NHF indicates that the company is not taking on any new customers for the time being as a result

Regarding Kogenate FS, the contact was not sure about the timing of Berkeley's planning to going into full production The source stated that NHF's understanding was that Bayer was still waiting on approval of a 200 liter fermenter NHF was not aware of Bayer's plans to build a European Kogenate manufacturing facility in Wuppertal Germany

The contact went on to discuss some background on NHF s position on Bayer Direct According to the source, Bayer notified NHF on Thursday August 31 2000 that Bayer Direct would be launched the following Tuesday, September 5, 2000 NHF had no prior

warning from Bayer regarding this program When asked if NHF had made any progress in persuading Bayer to modify the Bayer Direct program, the source stated that there remained "a wide chasm of disagreement" between the two parties

Analyst Comments

Bayer was granted approval of the Kogenate FS production in building 60 in an approval letter from the FDA dated June 26, 2000 The reference the source makes to Bayer awaiting approval of a 200 liter fermenter may be in error The analyst suspects that Bayer was actually telling NHF that they were awaiting approval of the entire production facility in building 60 Building 60 is made up of twelve 200 liter bioreactors (plus two spare 200 liter reactors) utilizing a new process technology that is significantly different from what Bayer had used in the past in producing Kogenate This will be verified in a future interview with this contact

Senior Operations Staff, Baxter Hyland Immuno

Interview: BHI2-2

Title: Senior Staff

Organization: Baxter Hyland Immuno

Background:

This source has a large network of contacts within the biotech industry and was contacted for an update on competitive capacity as well as information regarding the latest timelines for Baxter's rFVIII production facilities

Source comments

The source said that he had heard that Bayer's Berkeley plant had lost a lot of Kogenate FS due to mold problems

When asked about Bayer's plans for Wuppertal, the source indicated that if Bayer sticks to a fairly standard timeline they should be approved and capable of full production in 2005 This assumes 6 months to plan, 2 years to build, and 2 years to validate and approve the facility

Given that Bayer's stated capital outlay for Wuppertal is similar to Baxter's for Neuchatel, the source estimated that Wuppertal will have a capacity of between 750-1000 MAUs per year

Regarding Genetics Institute, the source stated that he is still hearing rumors that GI is planning to abandon the St Louis plant He noted that GI is building a new 220,000 square foot facility at its Andover Maryland campus However, the source was uncertain of this facility's purpose

Regarding the status of Baxter's Neuchatel plant, the source sta ed that hve cell cultures were to be run in November 2000 and conformance lots were planned for December 2000 or January 2001 In Thousand Oaks, suite B had received FDA approval and has already run 7 campaigns Thousand Oaks' suite C has run 5 campaigns anc is hoping to gain FDA approval within two weeks

The interview concluded with the source providing updated con act information for other Baxter operations staff personnel

Analyst comments:

The Kogenate FS lot referred to be the source may be either lo 670H076 or 670H071C which were voluntarily withdrawn by Bayer in late August 2000 due to low potency

Senior Marketing Staff, Baxter Hyland Immuno

Interview: BHI2-3

Title: Senior Marketing Staff

Organization: Baxter Hyland Immuno

Background:

This source has access to competitive pricing information from the field sales force [illegible] this source is knowledgeable regarding the typical dosing regimens for hemophilia patients

Source comments

The source provided the following pricing information for Kogenate FS

Pricing category	*Cost per unit*
Average Wholesale Price	$1 28
Direct-to-Patient	$1 13
PHS	$0 99

The conversation then turned to the typical dosing regimens for hemophiliacs being treated with rFVIII The source indicated that on-demand patients typically use rFVIII once per month at a dosage of 50 units/kg In the case of prophylactic patients the dosage regimen is typically 25-40 units/kg

Analyst comments:

The PHS pricing for Kogenate FS has been recently reduced (according to NHF sources) to 96 cents per unit

The dosage regimen information and pricing was used by the analyst to construct a supply model for Kogenate FS using dollar sales projections supplied by Bayer This is to be included in the final report of this project as an addendum

Senior Staff, National Hemophilia Foundation, Washington, DC

Interview: BHI2-4

Title: Senior Staff

Organization: National Hemophilia Foundation, Washington, DC

Background:

This source was contacted a second time for this project to clarify issues surrounding the pricing structure of Kogenate FS. Press releases by NHF had indicated that Kogenate FS was being sold at a 25% premium over the old formulation. Countering this has been repeated statements by Bayer that Kogenate FS is priced at the same level as the old formulation.

Source comments:

When asked to clarify the discrepancy between statements by NHF and Bayer regarding Kogenate FS pricing, the source indicated that the average wholesale price (AWP) for Kogenate and Kogenate FS was indeed, identical. This is why Bayer can claim that Kogenate FS is at the same price level as the old formulation. However, AWP is a somewhat arbitrary number, in that it does not reflect actual retail pricing of the product. Additionally, although the AWP is supposedly a wholesale price, the actual retail pricing of the product is less than AWP. The NHF source summarized the Kogenate and Kogenate FS pricing structure as follows:

Pricing category	*Kogenate (old formula)*	*Kogenate FS*
AWP	$1 28	$1 28
Non-PHS	$0 82	$1 13
PHS	$0 70	$0 96

The source pointed out that in the Bayer Direct distribution scheme patients would be charged at the non-PHS price level of $1 13 per unit versus the old non-PHS price level of $0 82 per unit In addition, Bayer is attempting to distribute Kogenate FS exclusively through Bayer Direct, which would translate into many more patients at the non-PHS price level

Finally, the source was asked the number of patients that NHF estimates Bayer serves with Kogenate each year The source indicated that although Bayer has given patient numbers ranging from 700-1700 patients, NHF estimates that Bayer actually has 3000 patients using Kogenate or Kogenate FS

The analyst brought up Bayer statements that they hope to enroll approximately 700 patients in Bayer Direct The source indicated that due to the negative publicity surrounding the Bayer Direct program, Bayer has only been able to enroll 70 patients in Bayer Direct as of late October 2000

Finally, the source was asked about NHF's information regarding the approval of Bayer's expansion suite in Berkeley The source indicated that the last word Bayer had given NHF, was that they were awaiting FDA approval of a new 200 liter bioreactor in Berkeley The analyst asked the source if it was possible that Bayer was awaiting approval on a *type of 200 liter reactor, not just a single, 200 liter unit* In other words, could it be possible that Bayer was actually awaiting approval for a group of 200 liter bioreactors? The source stated that this it was definitely possible that he had been mistaken in assuming that Bayer was only waiting approval of one, 200 liter bioreactor The source stated that he was not familiar with the details of the manufacturing facility in Berkeley and this could have caused him to make an incorrect assumption

Analyst comments:

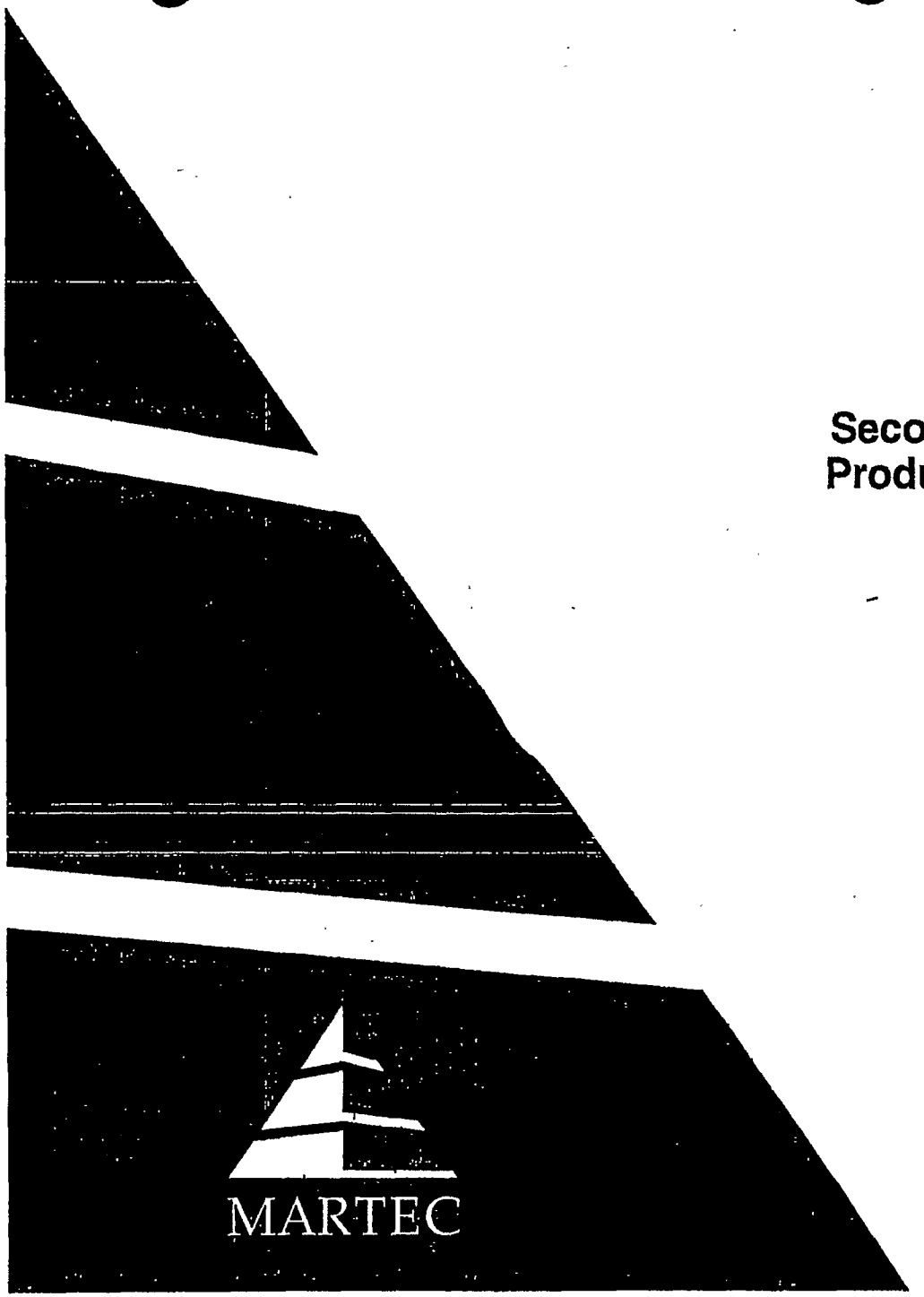
The new PHS pricing level of $0 96 is slightly lower than Baxter's last information placed this at $0 99 per unit.

The information on estimated number of patients that Bayer has using Kogenate and Kogenate FS will be used in the rFVIII supply model addendum to the final report of this project

2nd Gen. Recomb.

Product Intro

Assessment 7/98



Final Report

Second Generation Recombinant Product Introduction Assessment

Baxter Corporation

July 21, 1998

GH000836

Agenda

- **Objectives and Methodology**
- U.S. Findings
- European Findings
- Summary of Findings
- Conclusions and Recommendations

MARITZ

Introduction

The purpose of this report is to summarize the project findings, including:

1 A review of project objectives and methodologies

- Including a respondent listing

2 A summary of U S and European findings

- Patient, physicians and nurses *(U S only)*
- By European country, where appropriate

3 Strategic conclusions and recommendations

MARTEC

The primary goal of this project is to provide market intelligence allowing Baxter to successfully position its Factor VIII replacement products versus competitive next generation recombinant products.

Objectives

The two primary objectives of this project are:

- Understand the perceptions of decision makers on the next generation recombinant products (Kogenate SF and Refacto) coming to market
- Determine the motivators and drivers of switching behavior. What will cause and prevent switching from Recombinate to a competitive product?

Specific project objectives include:

1. Identify and determine the relative importance of key purchase criteria for Factor VIII replacement products
2. Understand strengths, weaknesses and differentiating features for all current products
3. Identify current unmet needs
4. Detail the switching environment for these products
5. Estimate likelihood of switching from Recombinate to new recombinant products
6. Analyze findings overall and segmented by world region and patient demographics

MARTE(

This project was conducted globally and consisted of two distinct phases.

Methodology

Global Scope

The project was conducted concurrently in both the United States and Europe The countries included in this study were·

- United States
- Germany
- France
- Italy
- Sweden
- Denmark
- UK*
- Spain*

**Added for Phase II*

Phase I

Phase I was a focused qualitative phase. Information was gathered primarily via in-depth one-on-one interviews The goal of this phase was to gain a qualitative understanding of the objectives This provided the foundation for the quantitative research phase

Phase II

This phase was a quantitative effort, with information gathered via telephone interviews This phase provided a detailed understanding of the project objectives and will provide Baxter the necessary foundation for developing effective market positioning strategies

MARTEC

GH000840

Approximately 300 interviews worldwide were completed for this study.

Methodology

Phase I and II Interviews*

Country	Respondent Group	Phase I Interviews Completed	Phase II Interviews Completed
U.S.	Physicians/nurses	10	60
	Patients	10	80
	Third Party Payers	5	--
Germany	Physicians	1	4
	Patients	2	11
France	Physicians	4	7
	Patients	2	10
Italy	Physicians	3	15
	Patients	2	6
Sweden	Physicians	3	2
	Patients	2	7
Denmark	Physicians	3	--
	Patients	2	3
UK	Physicians	--	10
	Patients	--	10
Spain	Physicians	--	8
	Patients	--	12
Total		49	245

A full listing of professional respondents is provided in the Appendix

Agenda

- Objectives and Methodology
- **U.S. Findings**
- European Findings
- Summary of Findings
- Conclusions and Recommendations

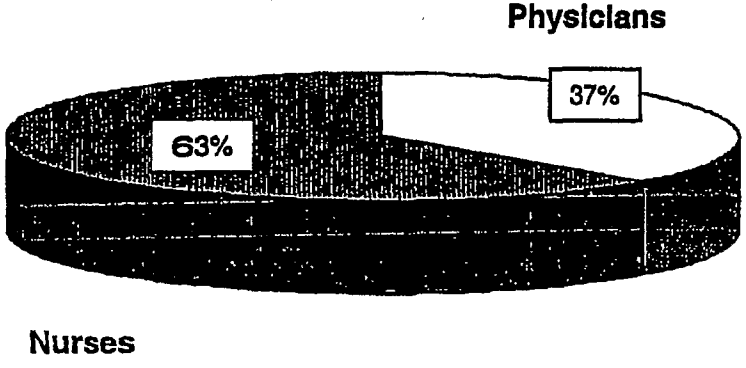
MARTEC

Of the 300 interviews completed worldwide, a total of 140 Phase II interviews were completed in the U.S.

U.S. Final

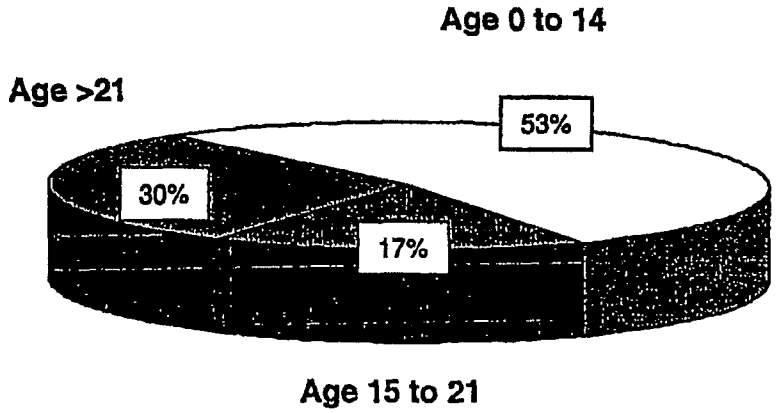
U.S. Respondents - Phase II -

Professionals



n = 60

Patients



n = 80

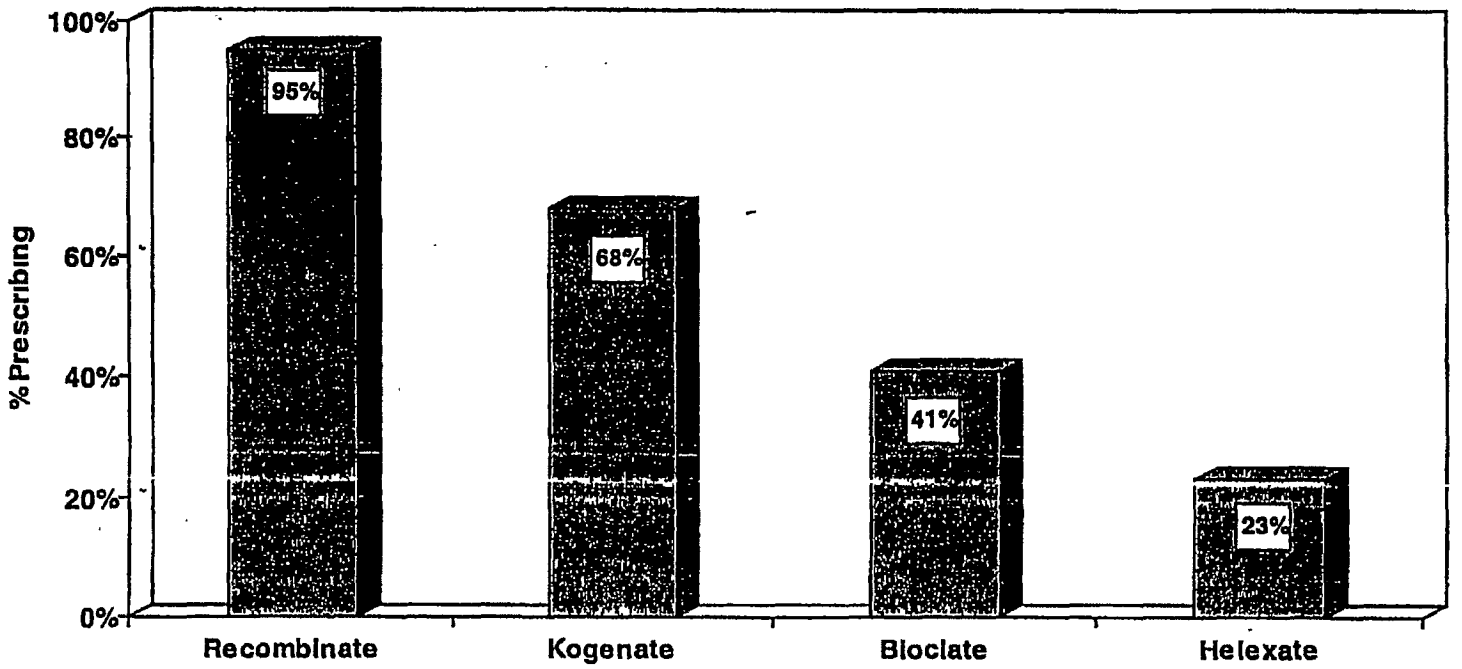
MARTI (

1

In the U.S., Recombinate is the Factor VIII replacement concentrate prescribed by the most physicians.

U.S. Final

Product Type Prescribed
- Physician -



MARTEC

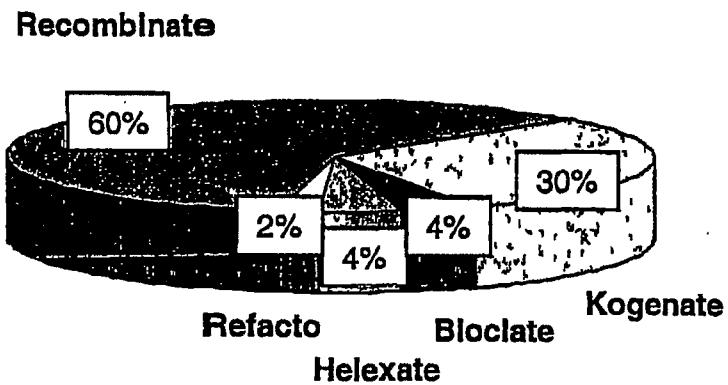
GH000844

In the study sample, more patients use Recombinate than any other product. Seventy-five percent of all respondents have switched products at least one time.

U.S. Final

Product Usage
- Patients -

Current Products



n = 80

Previous Products

Monoclate – P	34%
Others	14%
Don't know name	13%
Recombinate	9%
Hemophil M	5%
Bioclate	5%
Helexate	4%
Kogenate	4%
Reported no switching	*25%*
• *Ages 0-14*	*39%*
• *Ages 15-21*	*15%*
• *Ages 22 +*	*8%*

MARKET

The promise of improved *product safety* was the number one reason for switching products. Doctors provided the greatest influence in a patient's decision to switch.

U.S. Final

Reasons for Past Switching - Patients -

Safer product - less exposure to human protein	***49%***
Availability	14%
Doctor recommendation	12%
Efficacy	11%
Unit dosage size	8%
Developed inhibitor	6%
Developed viral infections	6%
Adverse side effects	5%
Clotting time	5%
Price	3%
Changed healthcare provider	3%

Past Switching Influencers - Patients -

Doctor	***43%***
Own research	24%
Pharmacist	10%
Hemophilia Treatment Center	10%
Nurse	7%
Parents/family	7%
Other patients	5%
Insurance	2%

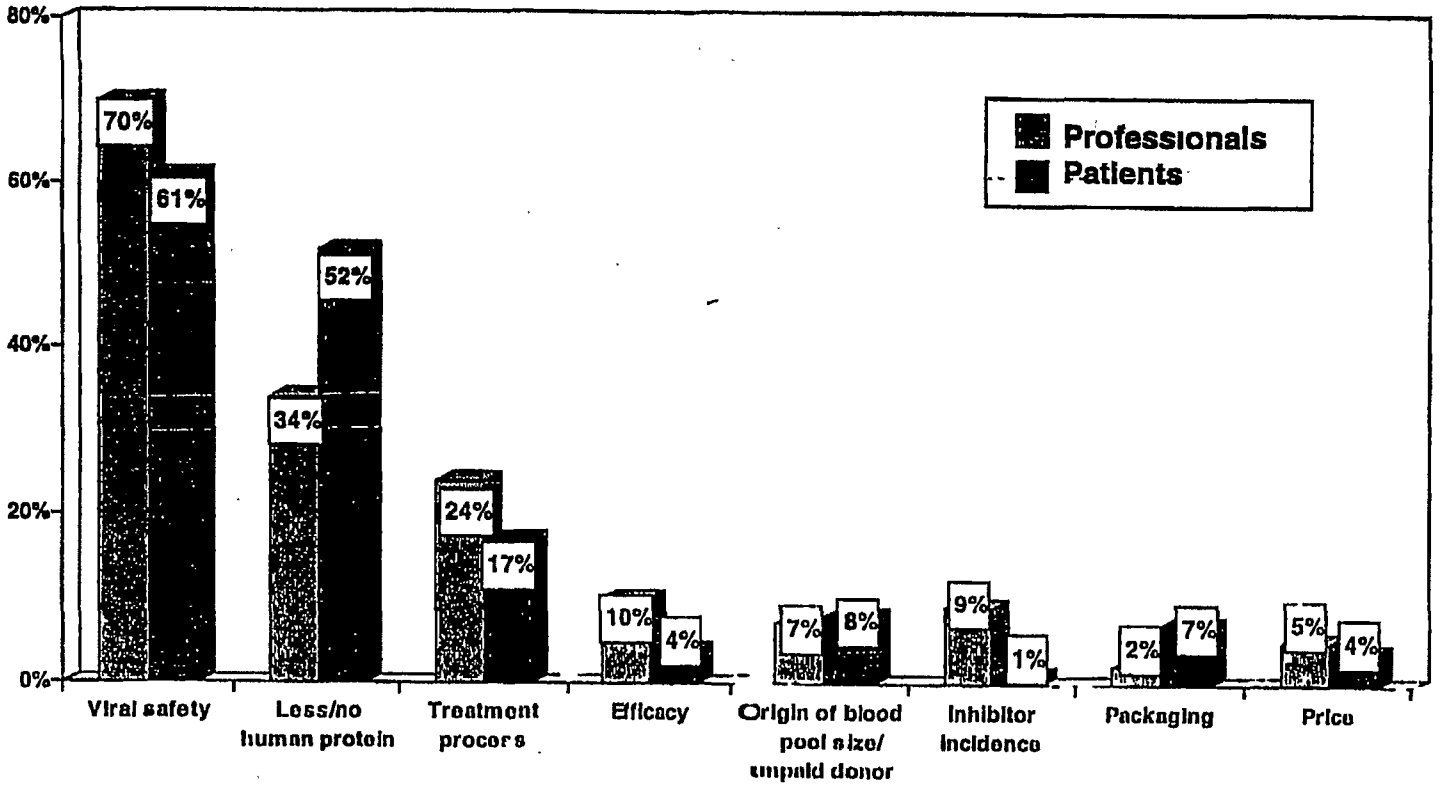
MARTEC

GH000846

Viral safety, level of human protein **and** ***treatment process*** **were most often mentioned as key elements of safety by both healthcare professionals and patients.**

U.S. Final

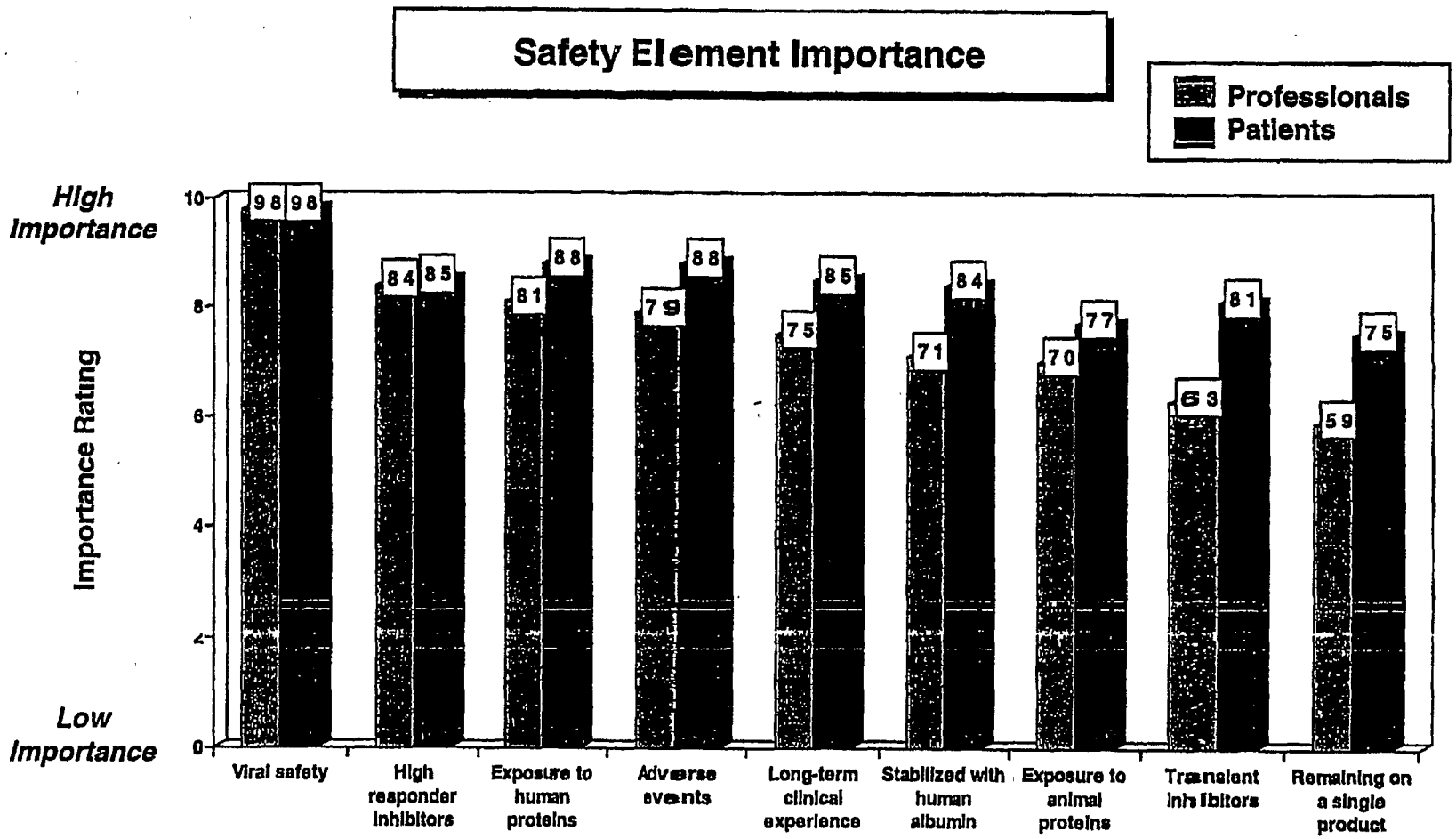
Unprompted Elements of Safety



MARKET

Viral safety **rated the highest in terms of safety importance for both groups.** ***Remaining on a single product*** **rated the lowest in importance.**

U.S. Final

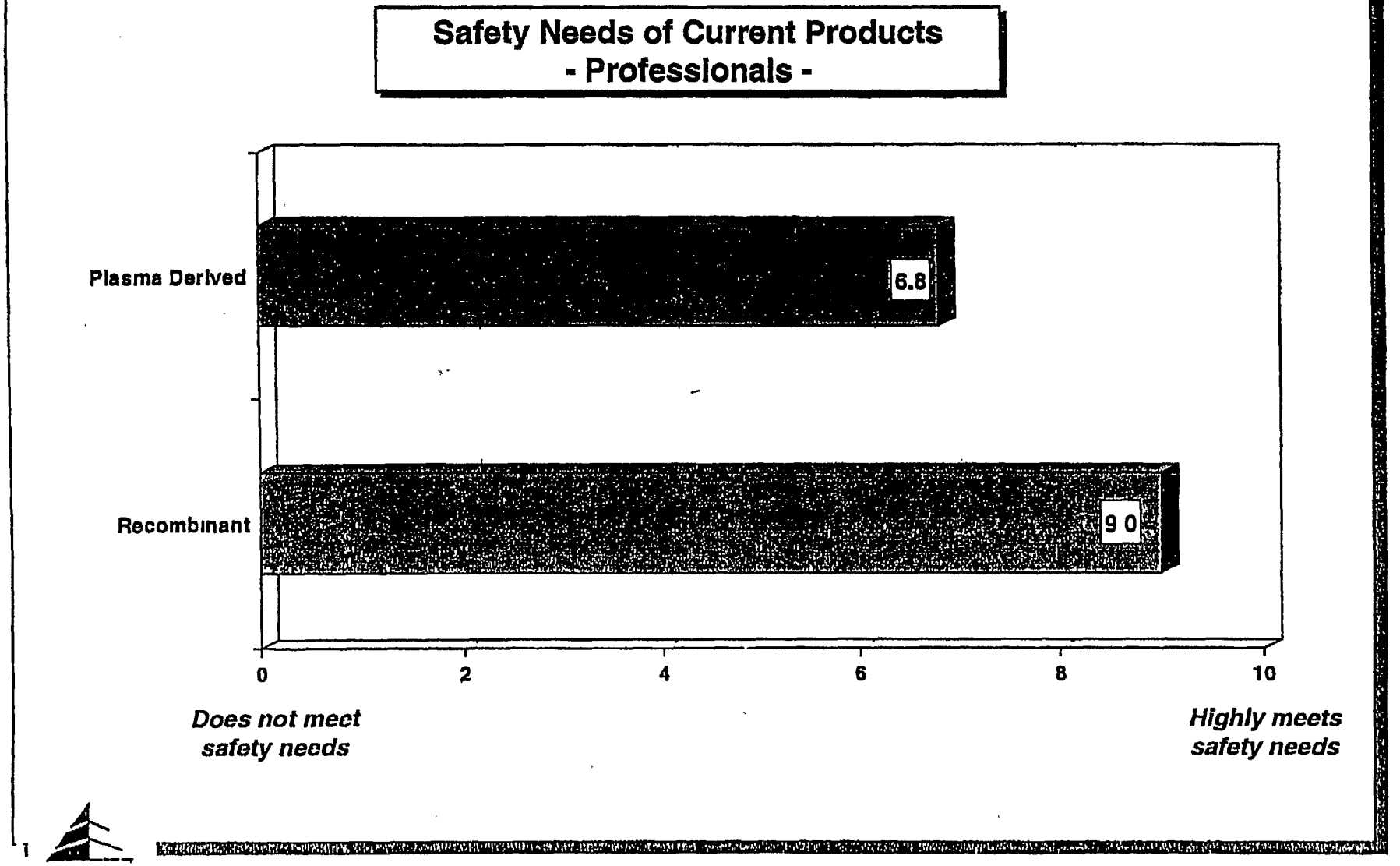


MARTEC

GH000848

Recombinant products are perceived by U.S. physicians and nurses as being much more able to satisfy patients' safety needs.

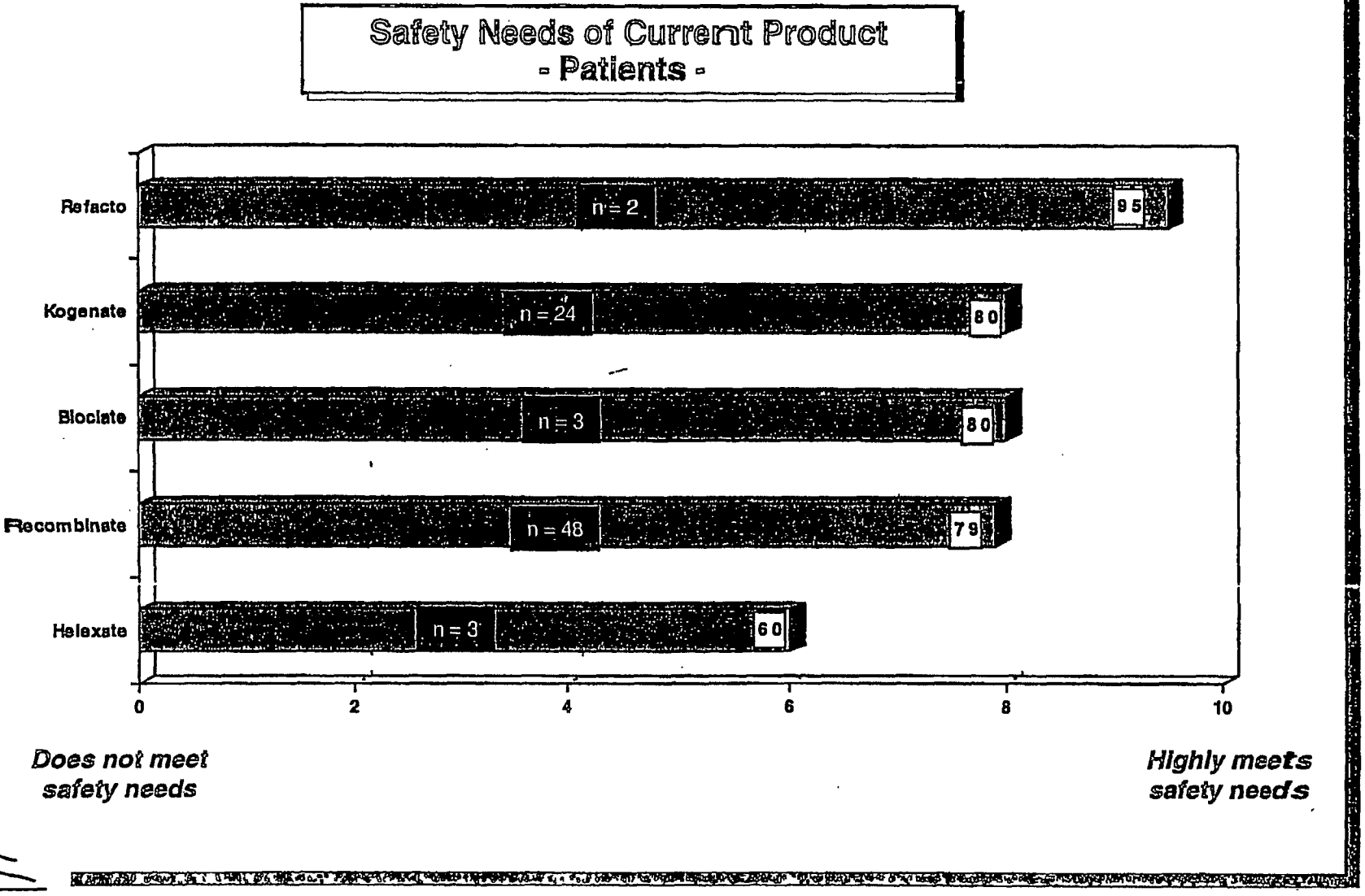
U.S. Final



MARTEC

Patients rated Kogenate and Recombinate nearly equal in terms of meeting their safety needs.

U.S. Final

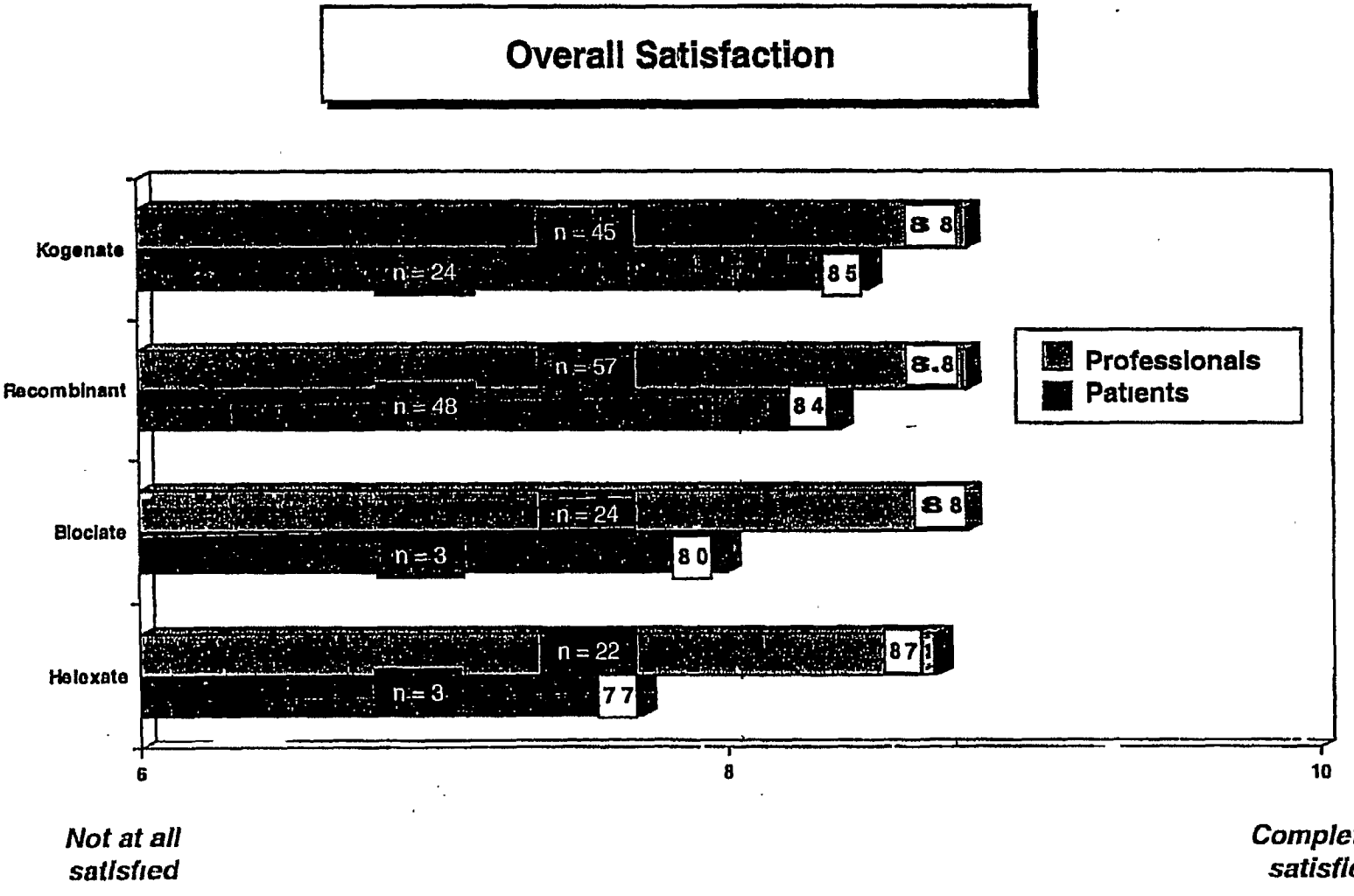


MARTEC

GH000850

Professionals are equally satisfied with all products. Patients are more satisfied with Kogenate and Recombinate than with other products.

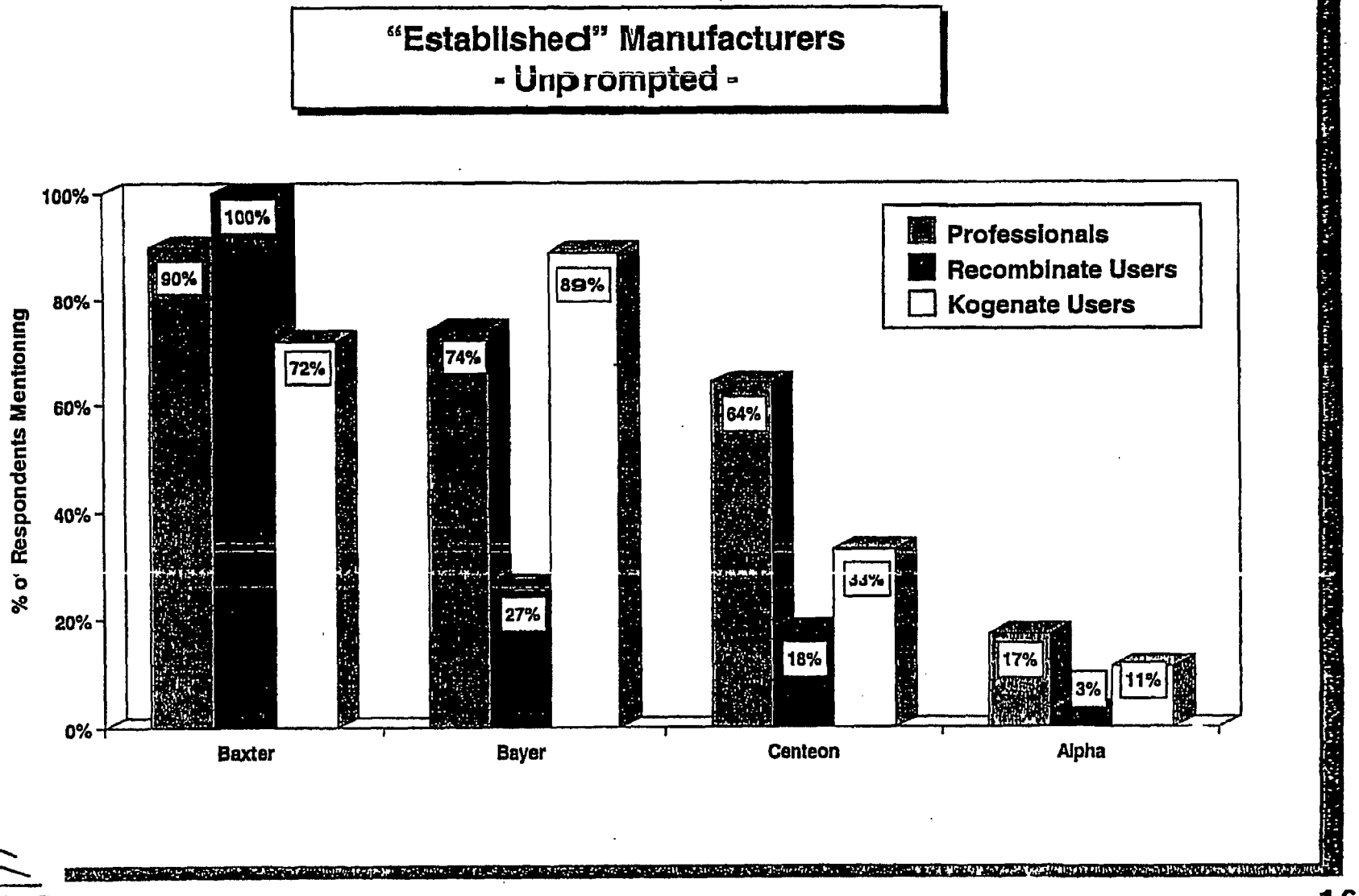
U.S. Final



MARH C

Baxter was most often thought of as an "established' manufacturer of hemophilia products. Few Recombinate patients mentioned other manufactures.

U.S. Final

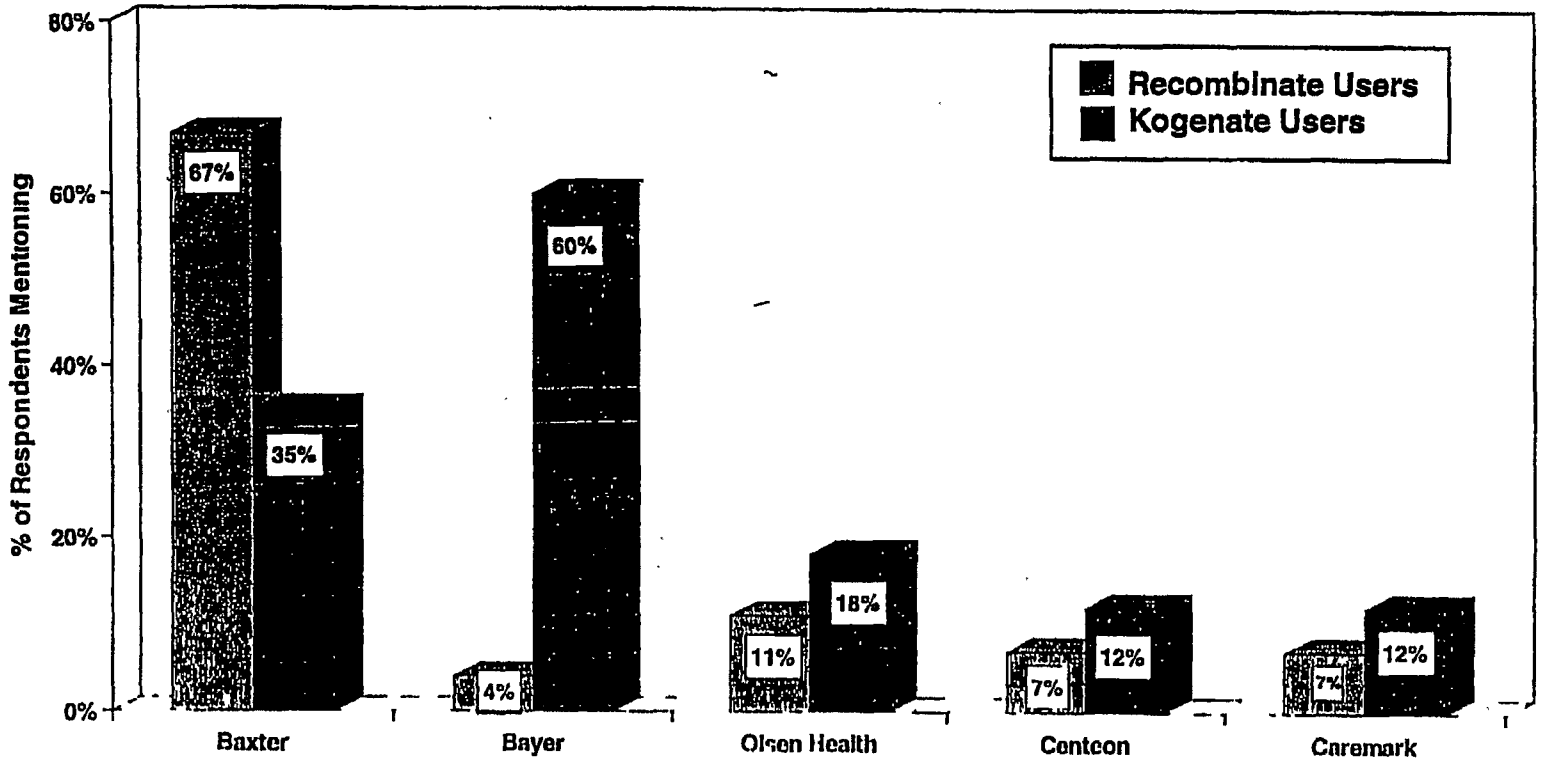


MARTEC

Only 4% of current Recombinate patients feel comfortable with Bayer as a supplier of their hemophilia products.

U.S. Final

Comfort Level with Manufacturers
- Patients Unprompted -

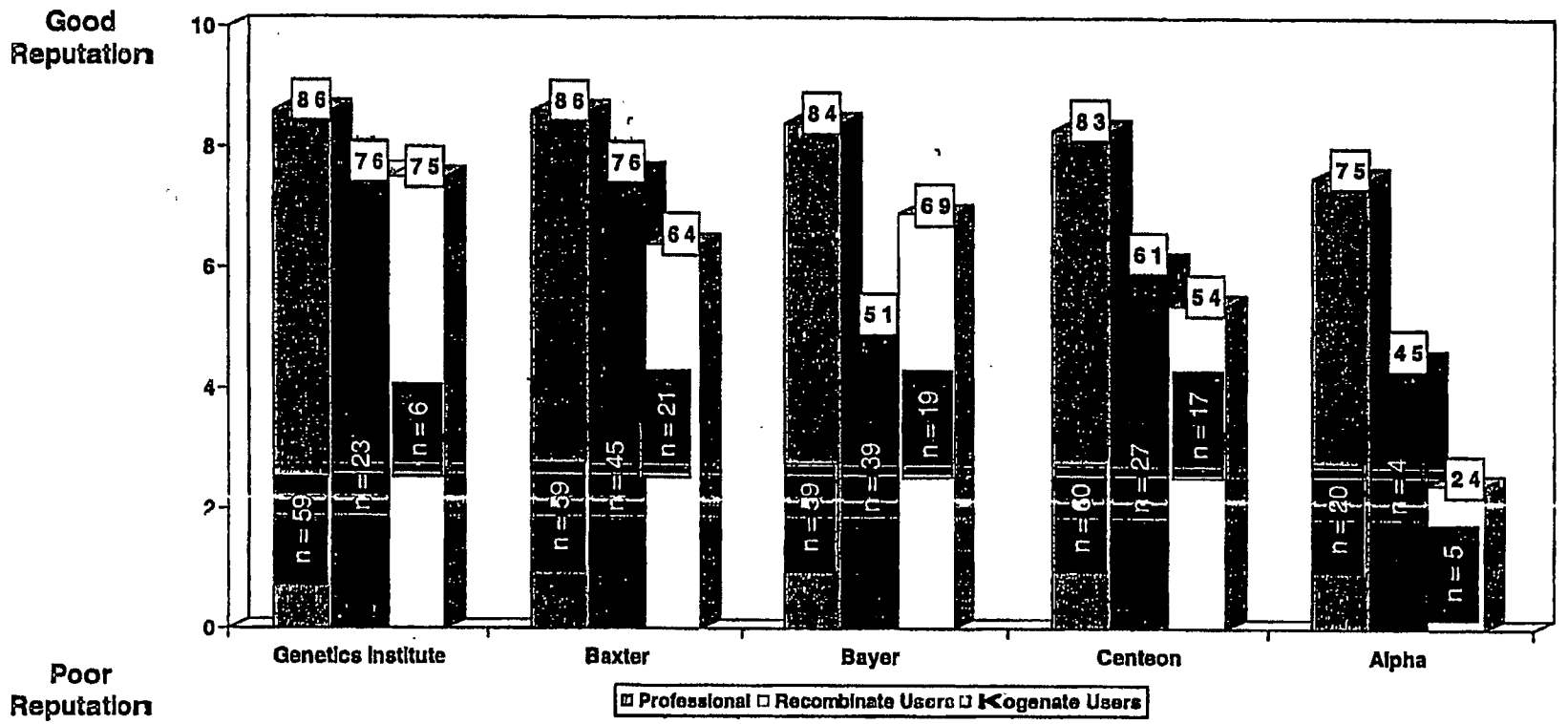


MARKE

Genetics Institute and Baxter are viewed as the companies with the best reputations.

U.S. Final

Company Reputation
- Prompted -



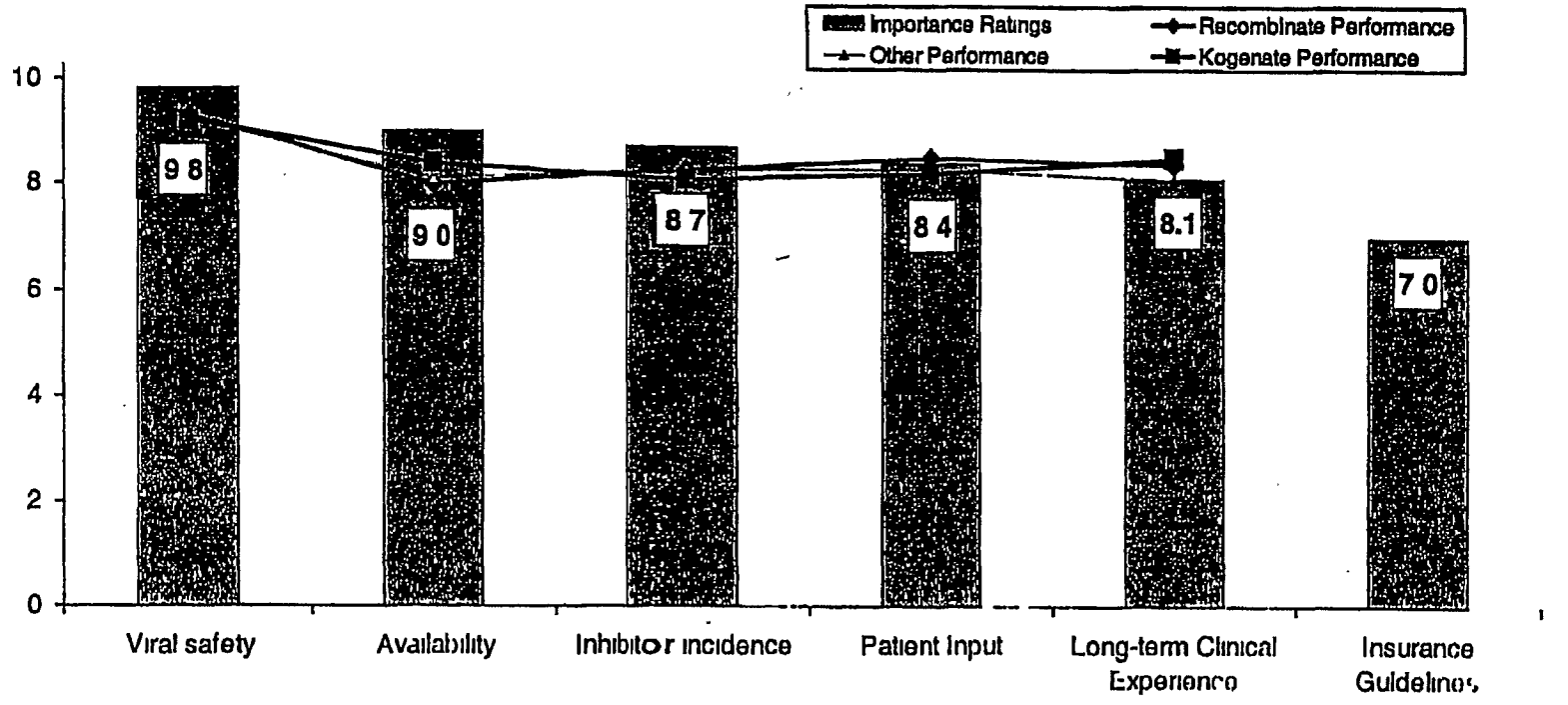
MARTEC

GH000854

Viral safety is clearly the most important key switching criteria. As for product performance, professionals view all products as equal.

U.S. Final

Professional Key Switching Criteria - Importance and Performance -



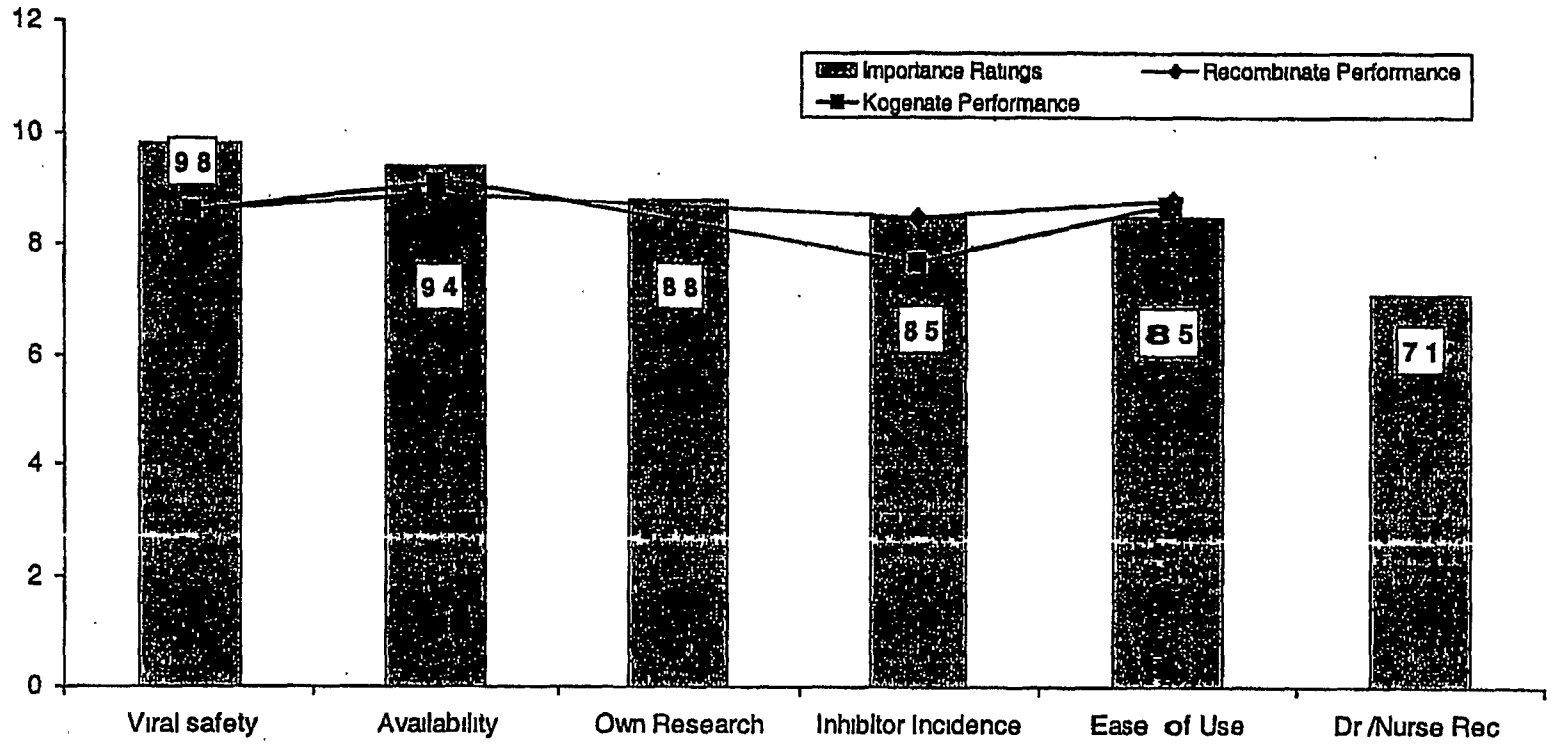
Performance was not asked for on Insurance Guidelines

MARIA

As with physicians, patients clearly rate *viral safety* as being the most important. Regarding product performance, patients claim Baxter outperforms Bayer in *inhibitor incidence*.

U.S. Final

Patient Key Switching Criteria
- Importance and Performance -



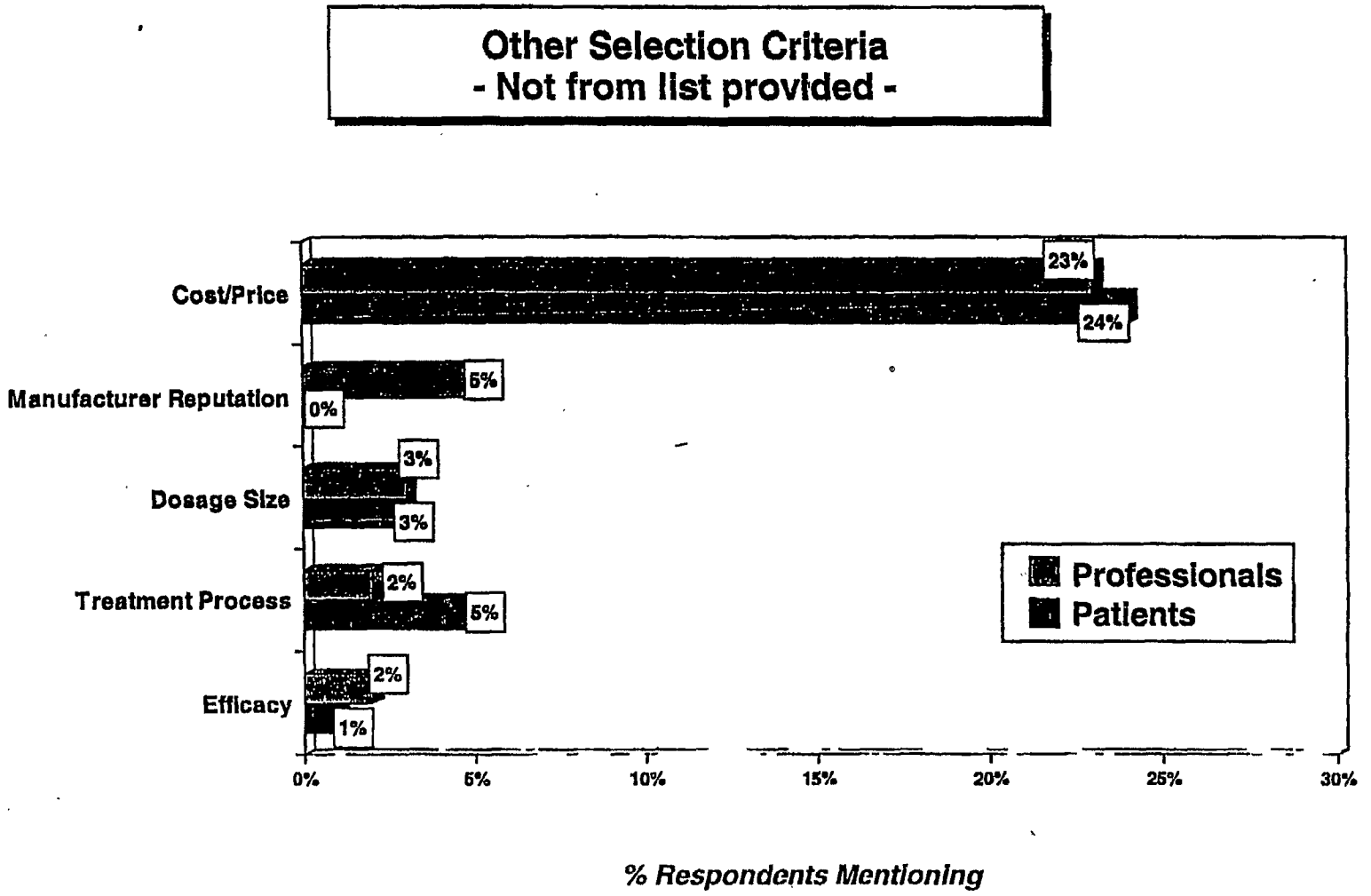
Performance was not asked for on Own Research and Dr /Nurse Recommendation

MARTEC

GH000856

When asked about other selection criteria not on the previous list, one quarter of respondents mentioned *cost*.

U.S. Final

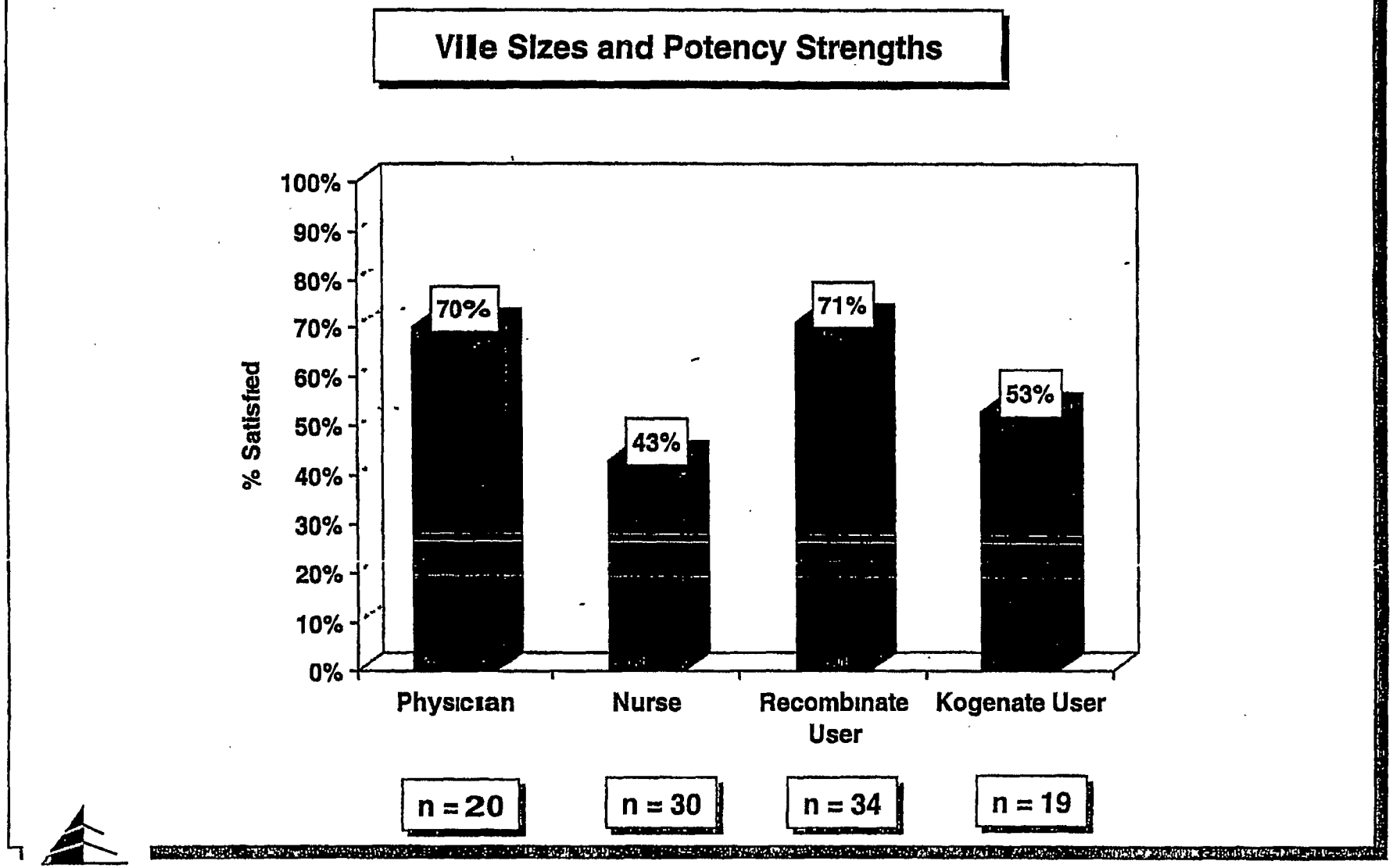


MARTEC

GH000857

Recombinate users and physicians claim to be the most satisfied with current vile size and potency strength options.

U.S. Final



MARTEC

GH000858

The two greatest concerns regarding vile sizes are *limited increment range* and *lack of availability* for existing sizes.

U.S. Final

Vile Size Improvements

Professionals

Desired Vile Sizes	Greater Availability
750 units - 8%	250 units - 16%
2000 units - 8%	500 units - 12%
1500 units - 6%	1000 units - 8%
100 units - 4%	
200 units - 4%	
125 units - 2%	
300 units - 2%	
4000 units - 2%	

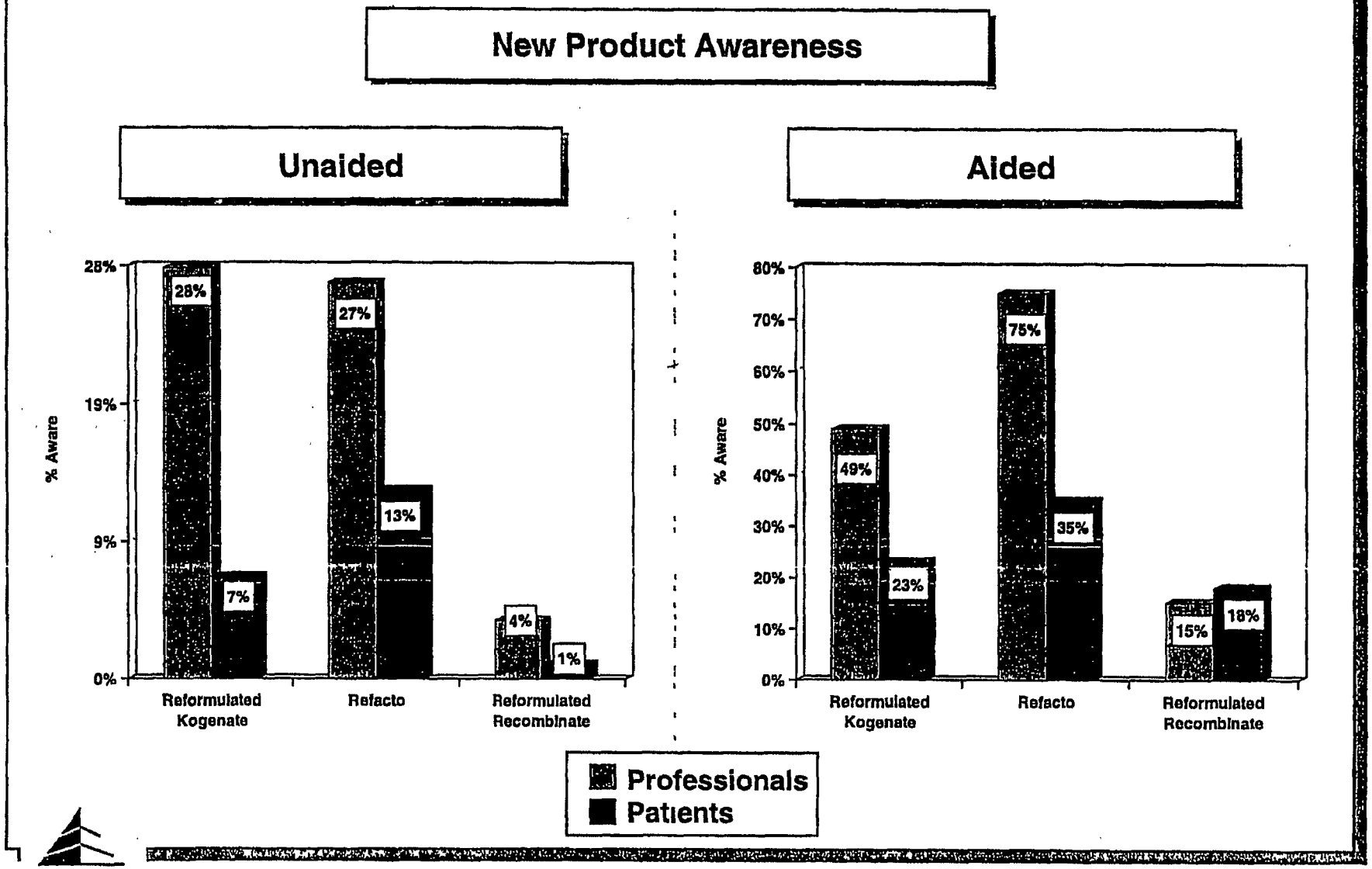
Patients

Desired Vile Sizes	Greater Availability
300 units - 4%	500 units - 16%
1600 units - 4%	1000 units - 12%
1800 units - 4%	
3000 units - 4%	
1300 units - 2%	
1400 units - 2%	
1500 units - 2%	
2100 units - 2%	
2500 units - 2%	
4000 units - 2%	

MARII (

Professionals are more knowledgeable of new products coming to market than patients. Refacto has the highest share of awareness in the U.S.

U.S. Final

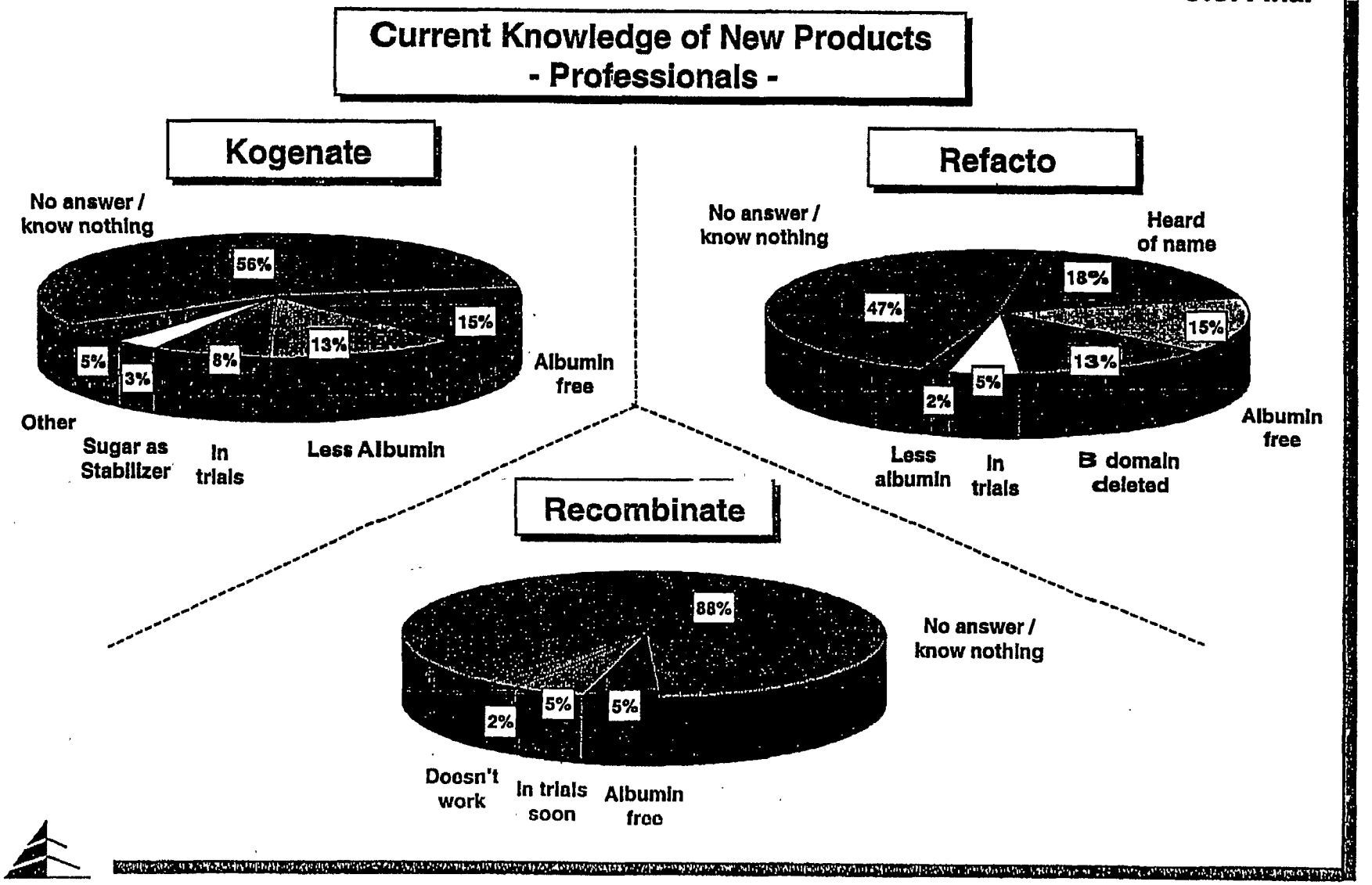


MARTEC

GH000860

U.S. physicians and nurses know the most about Refacto and reformulated Kogenate and the least about Recombinate II.

U.S. Final



MARKET

Even among U.S. professionals there is some misconception that the reformulated products will be albumin free.

U.S. Final

Current Knowledge of New Products
- Professional Comments -

Kogenate SF

"It eliminates exposure to human and animal proteins "

"It will contain a miniscule amount of human albumin "

"It is going to have a sugar base as a stabilizer, but still will use albumin in the manufacturing process "

Recombinate II

"I heard from Baxter representatives that it is just around the corner I need to read more about it "

"I have heard that it does not work "

"I think it will be in clinical trials soon "

Refacto

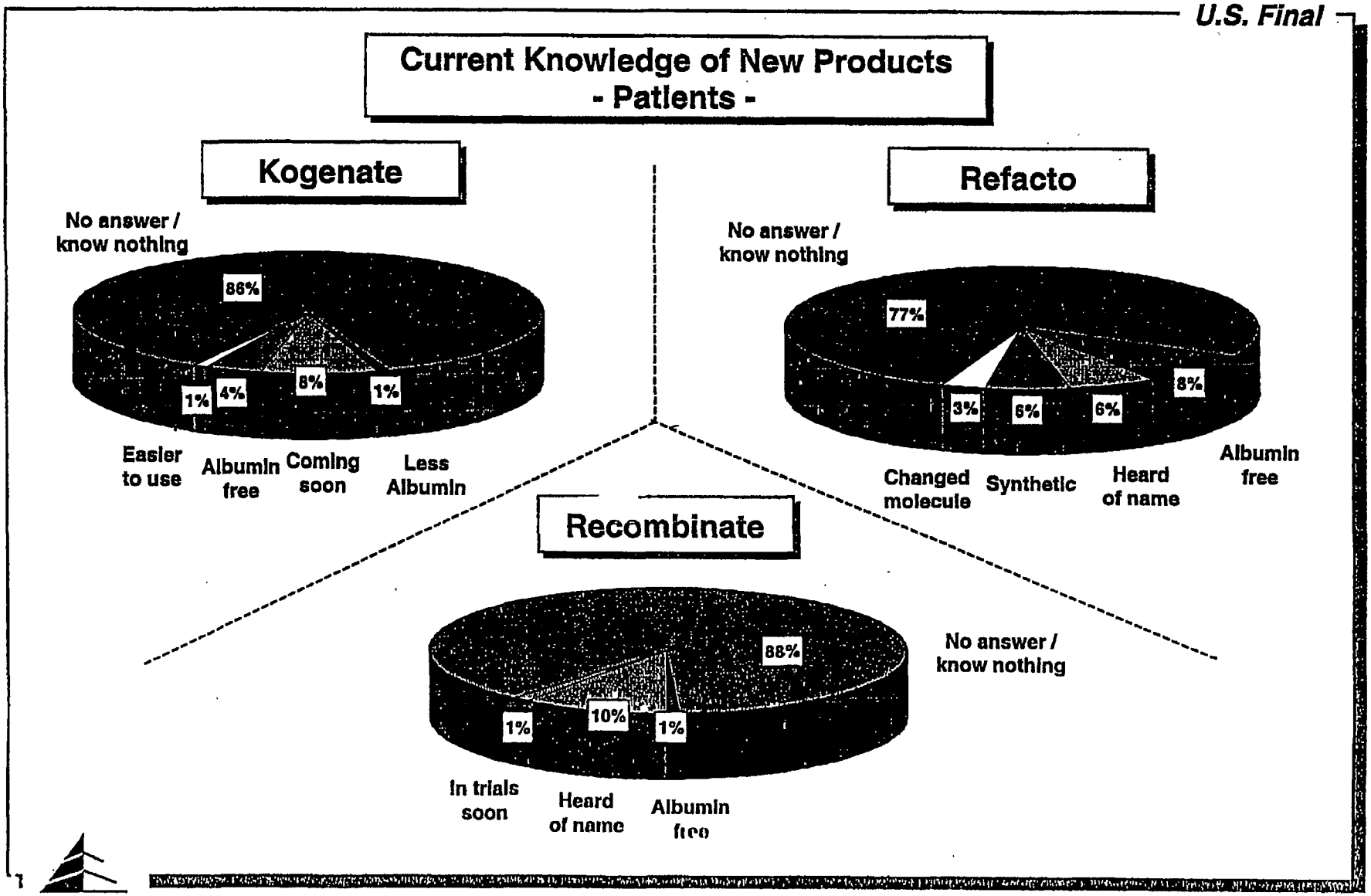
"It is b-domain deleted and originally contained no human albumin to reduce inhibitor incidence However, I heard it was unsuccessful at the last meeting I went to "

"I have a few patients on it right now It works really well and the patients like it "

"It is a b-domainless product and contains less albumin than the current recombinants "

MARTEC

U.S. patients know very little about any of the reformulated recombinant products.



MARTEC

Patient understanding of the reformulated products is limited.

U.S. Final

Current Knowledge of New Products - Patient Comments -

Kogenate SF

"It will have no albumin or human proteins "

"I don't know very much, just what I saw in the Hemophilia newsletter "

"I hear it will have lower amounts of human albumin "

Recombinate II

"I have heard of it, but don't know anything about it "

"I believe this is something that Baxter is working on "

"Some e-mail users have asked questions about this product I know nothing about it "

Refacto

"It is 100% synthetic using no blood products or albumin to stabilize it It causes more inhibitors, but has no adverse reactions, works fast in response to bleeds and is in smaller concentrations "

"They have restructured the molecules and removed the albumin "

"They have applied with the FDA and it will be out in 3 months It is totally synthetic "

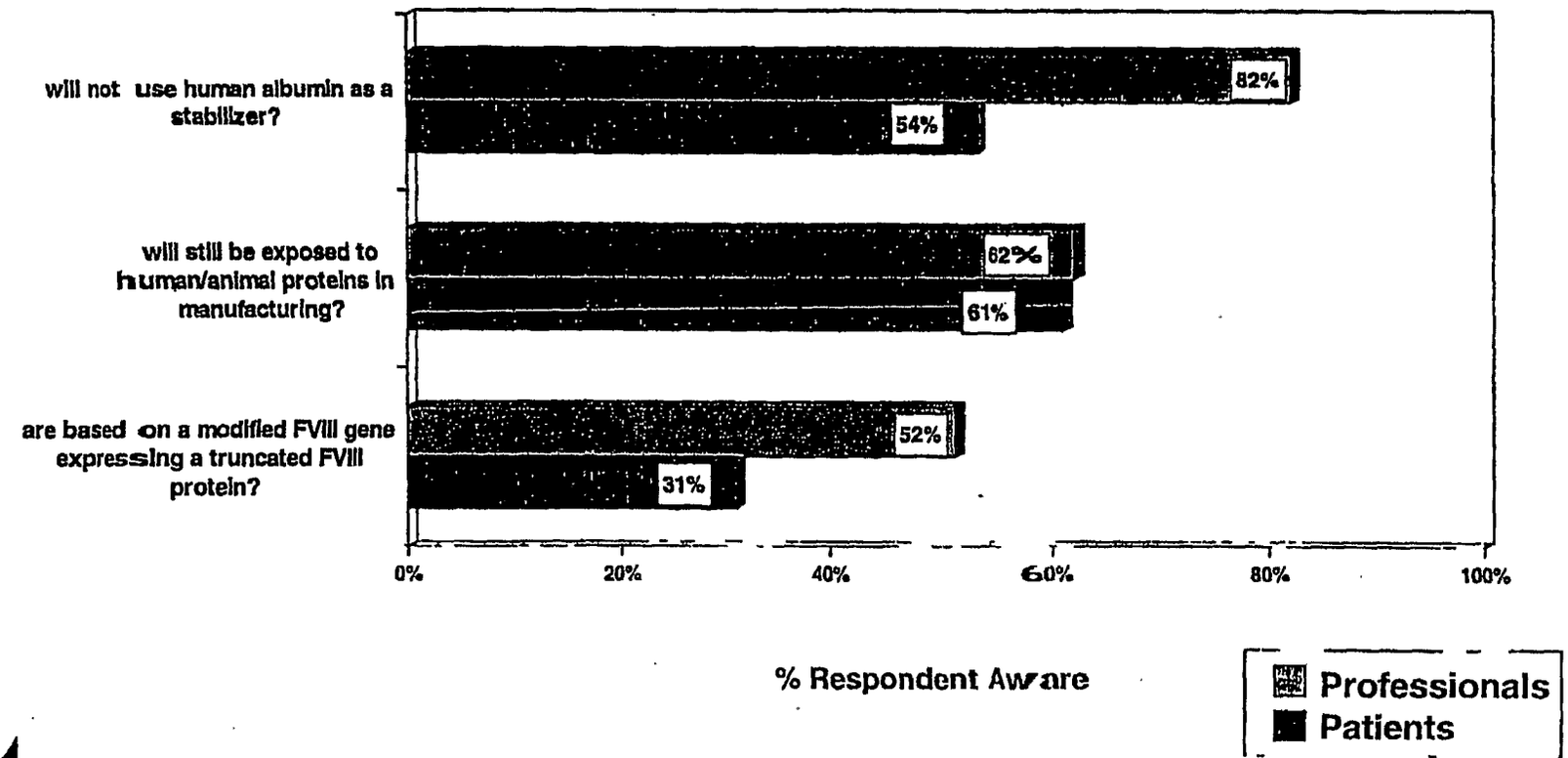
MARTEC

Professionals are fairly aware of the composition of the newly reformulated products. Patients knew the least about the use of a modified gene.

U.S. Final

New Product Awareness

Are you aware that certain reformulated recombinant Factor VIII concentrates . . .

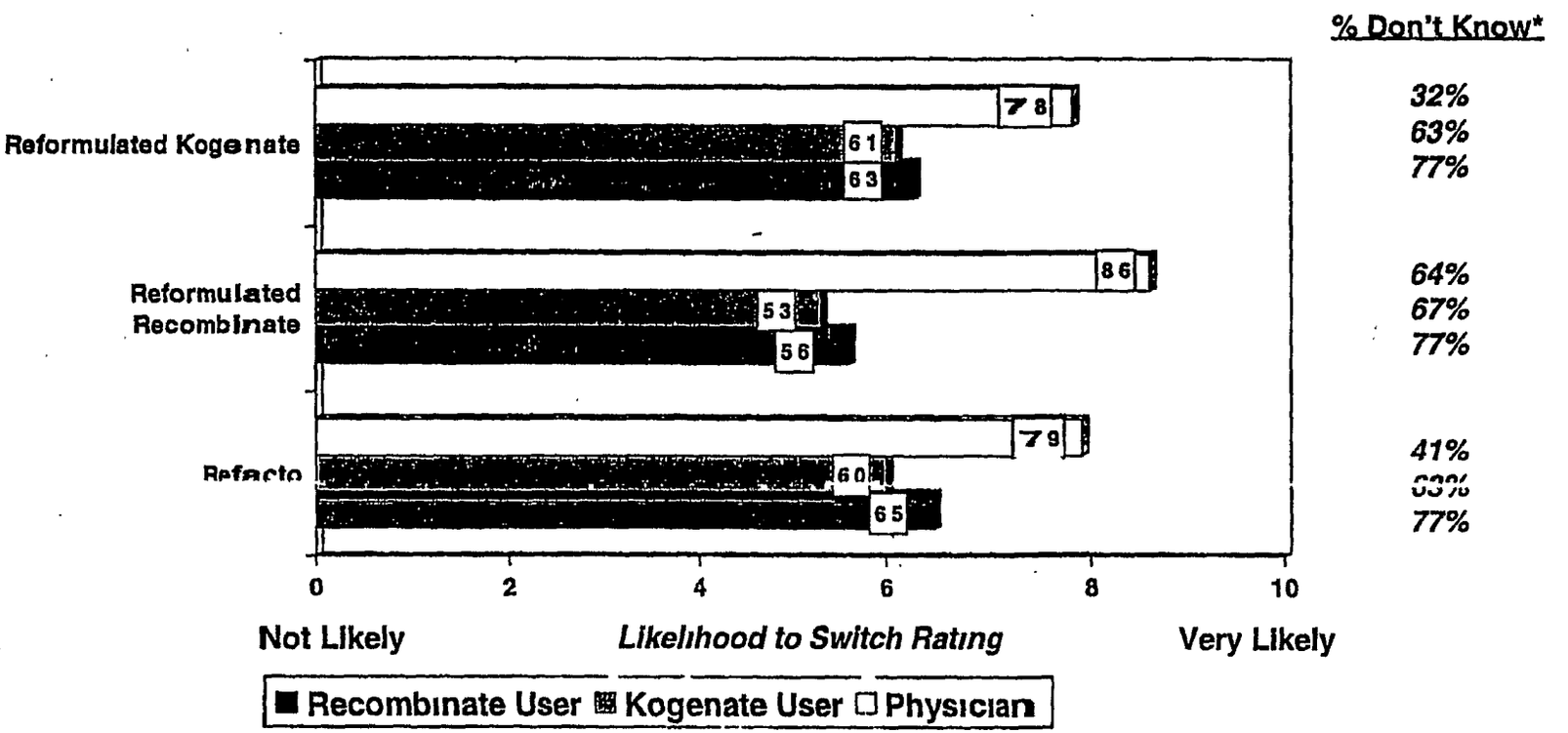


MARKET

The high percentage of "don't knows" indicates a need for more information before switching.

U.S. Final

Likelihood to Switch to Reformulated Product

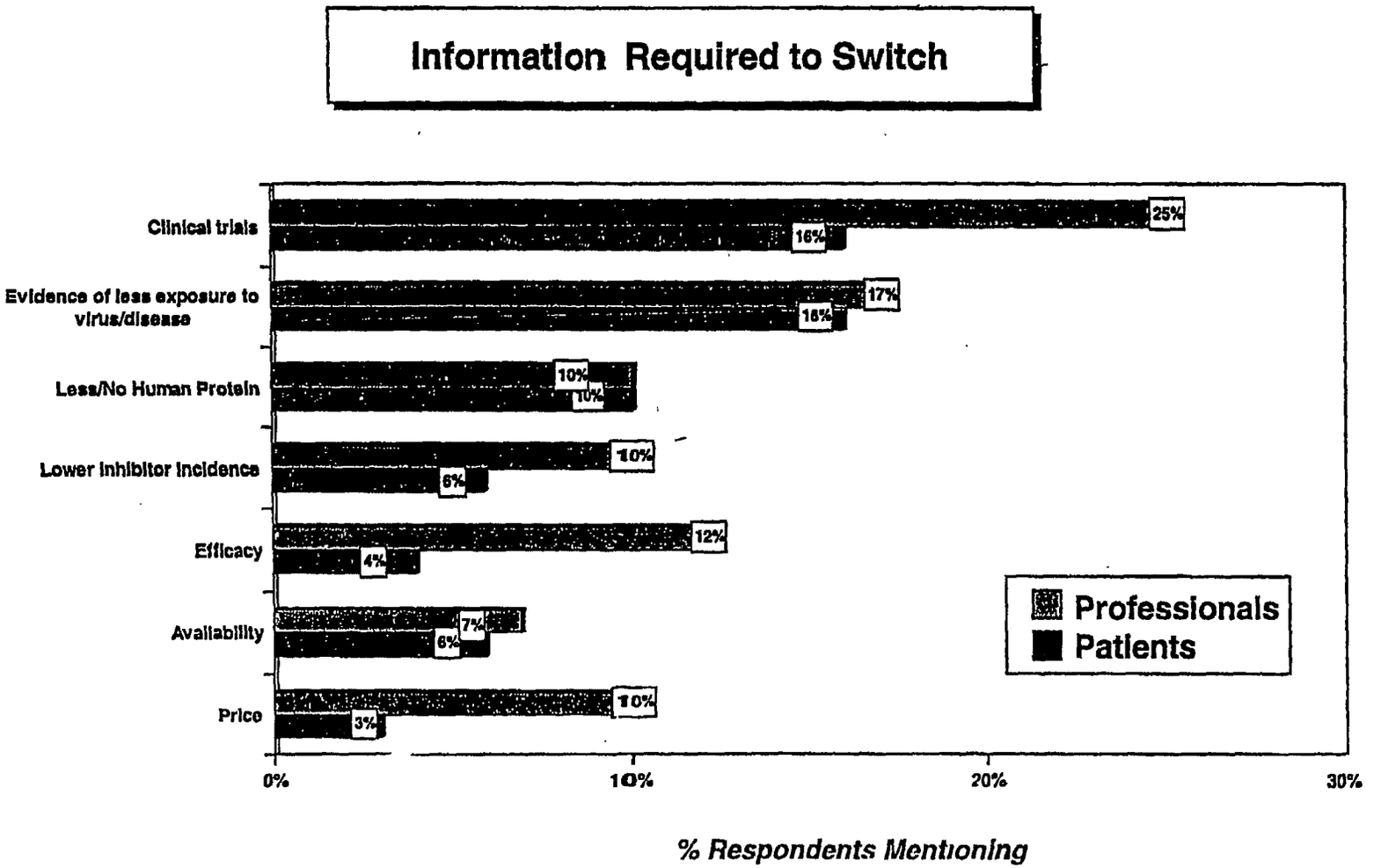


MARTEC

GH00O866

The U.S. hemophilia community needs to see *clinical trial results* with evidence of *improved viral safety* prior to switching to a refomulated product.

U.S. Final

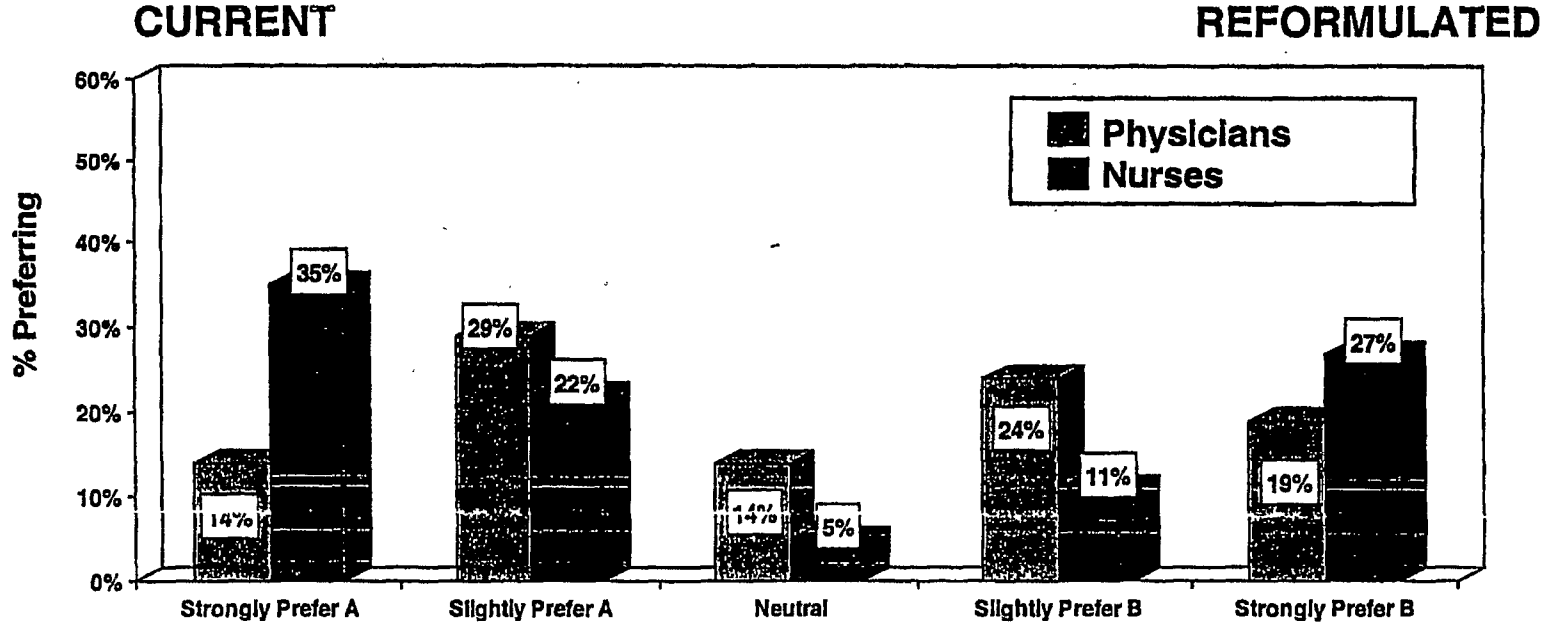


MARIT(

Nurses show a slight preference for a current Factor VIII concentrate over a reformulated one on the market for only six months, given the same manufacturer. Physicians are evenly divided.

U.S. Final

Product Trade-off
- Current vs. Reformulated -
Manufacturer and price are equal



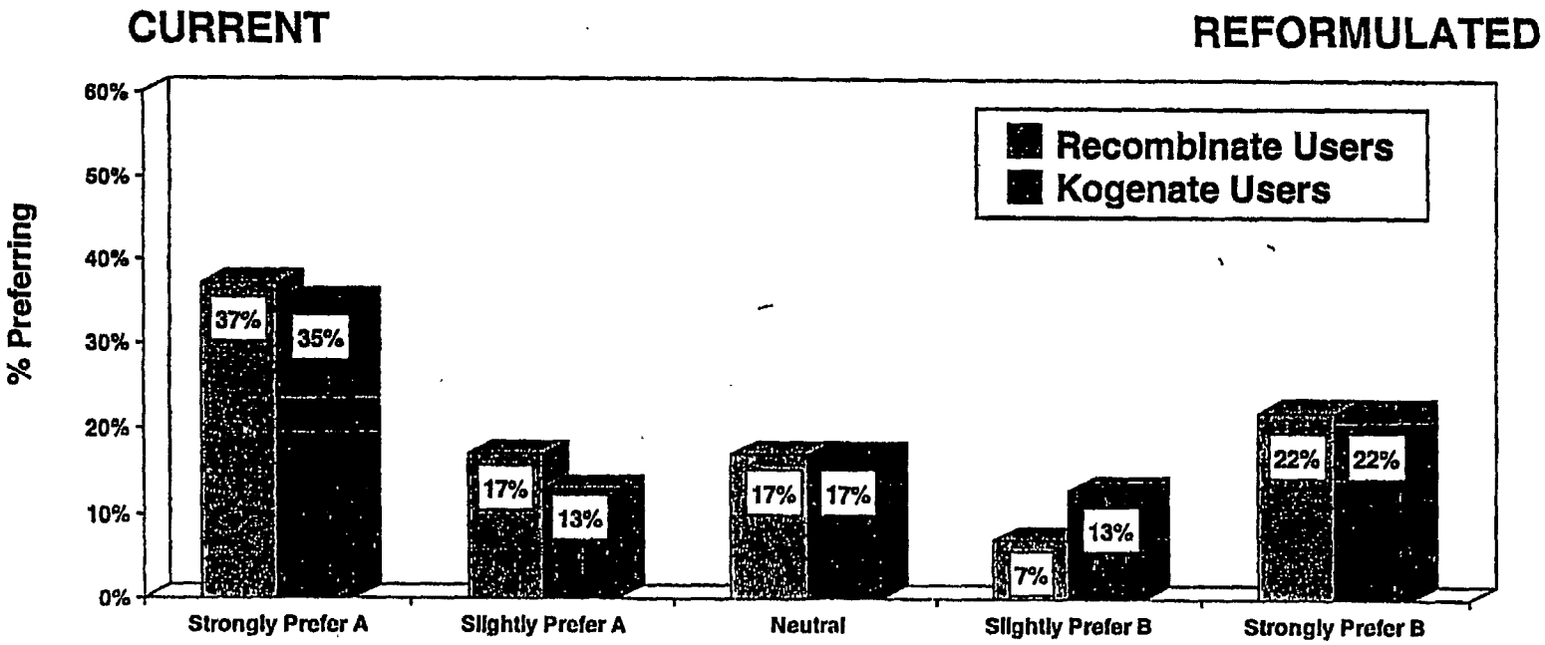
Product A	A current recombinant Factor VIII concentrate that has been on the market for six years
Product B	A reformulated recombinant Factor VIII concentrate that has been on the market for six months
Comments	Both are manufactured by the same company and cost the same

MARTEC

Patients also show a slight preference for a current Factor VIII concentrate over a reformulated one that has been on the market for only six months, given the same manufacturer.

U.S. Final

Product Trade-off
- Current vs. Reformulated -
Manufacturer and price are equal



Product A	A current recombinant Factor VIII concentrate that has been on the market for six years
Product B	A reformulated recombinant Factor VIII concentrate that has been on the market for six months
Comments	Both are manufactured by the same company and cost the same

MARKET

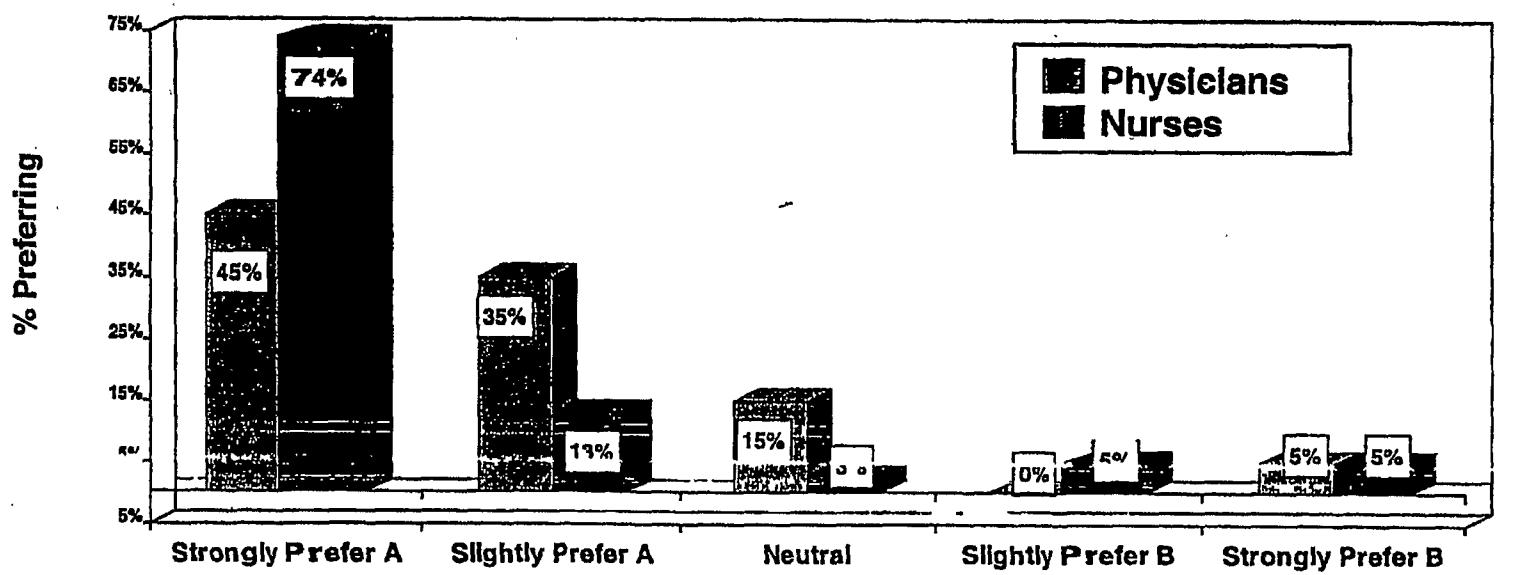
Nurses and physicians demonstrate a strong preference for a current product from an existing manufacturer over a reformulated product from a new manufacturer.

U.S. Final

Product Trade-off
- Current vs. Reformulated -
- Existing vs. New Manufacturer -
Price is equal

CURRENT
ESTABLISHED MFG.

REFORMULATED
NEW MANUFACTURER



Product A. A current recombinant Factor VIII concentrate that has been on the market for six years

Product B: A reformulated recombinant Factor VIII concentrate that has been on the market for six months

Comments. Product A is manufactured by the company that is established as a manufacturer of recombinant Factor VIII concentrates Product B is manufactured by company with no experience with Factor VIII concentrates Both cost the same

MARTEC